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TRANSACTIONS & STUDIES
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(June 1957)

The Pathogenesis of Uterine Carcinoma; Cervical and Endometrial[1]

By ARTHUR T. HERTIG, M.D.[2]

INTRODUCTION

THE two main forms of uterine cancer, squamous carcinoma of the cervix and adenocarcinoma of the endometrium, present a series of contrasts. Such contrasts are seen whether one considers the type of patient in which the two diseases occur, the environment in which they begin, their age of onset, incidence, pathogenesis, biologic course, method of therapy or prognosis.

Briefly, cervical carcinoma tends to occur in patients who have been married or have had coitus prior to age 20, delivered a baby prior to age 21 and whose husbands are uncircumcised or whose penile hygiene is poor. Although certain ethnic and racial groups may be more or less susceptible to the disease, the factors of penile hygiene could be the explanation for the greatly reduced incidence of the disease in Jewesses and the significantly greater incidence in Negresses. That all these factors are probably of varying but unproven importance is shown by the virtual absence of cervical cancer in nuns, although the latter have the expected incidence of cancers at other sites.

On the other hand, endometrial carcinoma tends to occur in patients whose endocrine background is abnormal. They marry later or much less frequently and when married are more often sterile or produce fewer children than do their sisters who have cervical cancer. Moreover, they are often obese, relatively prone to develop diabetes, breast cancer and hyperthyroidism. As evidence of their endocrine instability or "imbalance", they frequently have had abnormal ovarian function with associated endometrial hyperplasia and meno-metrorrhagia prior to the development of endometrial neoplasia.

As one interested in the pathology of obstetrics and gynecology for the past 25 years, your essayist speaks on the observations made in the pathological laboratories of The Free Hospital for Women and the Boston Lying-in Hospital by him and his colleagues. The majority of these data have already been published with full illustration of the morphologic aspects. The significant biological, pathological and clinical features of cervical and endometrial carcinoma have also been compiled by Dr. Hazel Mansell and your essayist in the second fascicle on the "Tumors of the Female Sex Organs" now in press. It is part of a multi-authored *Atlas on Tumors* now being

[1] Mary Scott Newbold Lecture LXXIV, College of Physicians of Philadelphia, 5 December 1956.

[2] Shattuck Professor of Pathological Anatomy, Harvard Medical School, Boston, Massachusetts.

published by The National Research Council in collaboration with The Armed Forces Institute of Pathology. Its extensive bibliography precludes the necessity for one in this communication. Moreover, since these remarks will be made entirely from an extensive series of lantern slides, most of them photomicrographs which necessarily cannot be published in the *Transactions & Studies* of your College, this published version of the lecture is a summarizing description of the histological sequence of events leading up to cervical and endometrial carcinoma.

SQUAMOUS CARCINOMA OF THE CERVIX

It is generally agreed that this cancer arises at or near the squamo-columnar junction, *usually* on the endocervical or columnar epithelial side of this junction. Rarely a squamous carcinoma of the cervix arises *de novo* on the portio vaginalis from true squamous epithelium. That such epithelium probably plays little part in the genesis of the usual cervical carcinoma is shown by the fact that such cancers are about one-half as common in the prolapsed cervix. This is in spite of the fact that the latter is often subject to ulceration with its associated proliferative repair of squamous epithelium at the margin of the ulcer. Moreover, when carcinoma occurs in prolapsed cervices, it tends to arise at the squamo-columnar junction and is composed of non-keratinizing tumors as are the tumors which arise in the normally positioned cervix.

To explain the apparent discrepancy of a squamous carcinoma arising from a columnar mucous membrane—one must consider the series of changes known to occur during and after pregnancy. Eversion of the distal endocervical mucosa occurs so that the latter is now exposed to the vaginal canal with variable degrees of erosion, inflammation and squamous metaplasia taking place in the endocervix thus exposed. (That the squamous metaplasia may well have arisen on a hormonal basis due to the pregnancy is shown by the fact that normal newborns show comparable changes in their cervices.) Following delivery the cervix attempts to return to its pregravid state but the lacerations cause the endocervical eversion with its erosion, inflammation and metaplasia to persist to varying degrees. Such squamous metaplasia undergoes varying degrees of maturation and may even show disturbances of keratinization. It occupies the exposed endocervix with its underlying glands and may even extend up into the non-exposed portions of the endocervix. Although most cervices showing squamous metaplasia of the endocervix do not become the seat of neoplasia, evidence is gradually accumulating that on occasion (34 uterine cancers per 100,000 female population) such metaplasia gradually undergoes a malignant change. The precise length of time required for such malignant transformation is not known although it requires approximately 10–15 years for squamous carcinoma in situ of the cervix to progress to invasive carcinoma. The interval is suggested by age distribution curves of these two phases of the tumor (Fig-

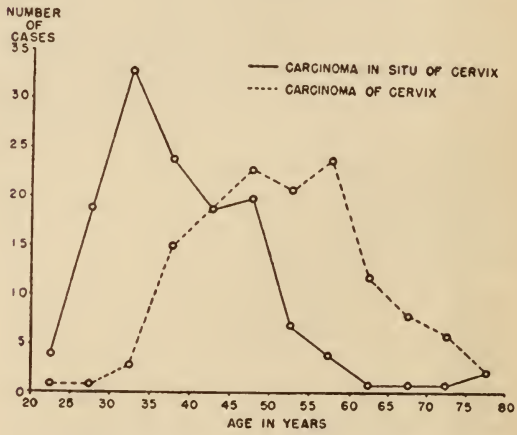

FIG. 1. Frequency distribution curves of 135 consecutive cases each of carcinoma in situ and carcinoma of the cervix at the Free Hospital for Women. The cases of carcinoma in situ were collected during the years 1916–1947, whereas the carcinomas were from 1941, 1942 and 7 in 1943. (These 135 cases of cervical carcinoma are not the same as the series on which Younge determined the average age as 48 years. This particular series has an average of approximately 50 years.) From "A Debate. What is Cancer in situ of the Cervix? Is It the Preinvasive Form of True Carcinoma?" Hertig, A. T. and Younge, P. A., Am. J. Obst. & Gynec., 64: 807–815, 1952.

FIG. 2. Pictorial representation of transition from benignancy to malignancy. Courtesy of Dr. Hugh Grady, Armed Forces Institute of Pathology, Washington, D. C.

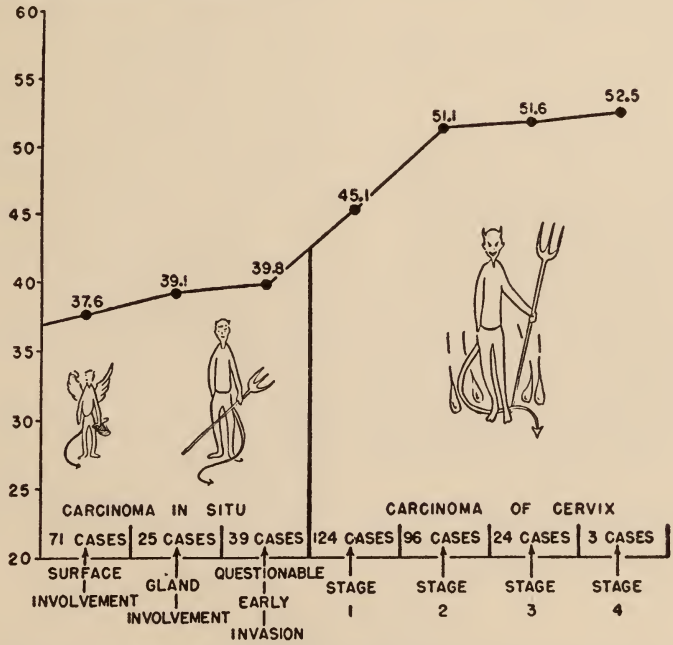

FIG. 3. Average ages of successively more advanced stages of cervical carcinoma from the in situ stage to League of Nations Stage 4. The little figures are copied from the last three on the right of Fig. 2 and represent varying stages of malignancy.

From "A Debate. What is Cancer in situ of the Cervix? Is it the Preinvasive Form of True Carcinoma? Hertig, A. T. and Younge, P. A., Am. J. Obst. & Gynec., **64:** 807–815, 1952." "Carcinoma in situ of the cervix: A General Consideration, McKelvey, J. L. Am. J. Obst. & Gynec., **64:** 816–832, 1952."

ure 1) and by the average age of groups of patients with varying stages of cervical cancer (Figures 2 and 3).

Although the morphologic sequence of events, progressing from metaplasia through varying degrees of anaplasia to neoplasia of the exposed endocervix, is not completely documented, the relationship of carcinoma in situ to invasive carcinoma has been extensively studied by many investigators in this country and in Europe during the past 40 years.

Carcinoma in situ may be defined as the presence of morphologically malignant but noninvasive squamous epithelium on the surface and/or in the glands of the cervix. That it is the probable precursor of invasive carcinoma is suggested by the following circumstantial evidence.

1. The incidence of the two conditions, although not equal is comparable: 0.053% and 0.034% respectively.

2. The average age at which it appears is

about 10 years earlier than invasive carcinoma.

3. Its occurrence in Jewish and Negro patients is comparable to that of invasive cancer in those two ethnic or racial groups.

4. The in situ stage of the disease has been observed to progress to the invasive form in from 5–12 years. (The author demonstrated one lesion which apparently evolved during 11 months of observation.)

5. In patients with cervical carcinoma prior biopsies taken 1–17 years before usually show the in situ stage of the disease.

6. Serial sections of cervices harboring carcinoma in situ reveal the lesion to be actually invasive in from 5–23% of cases.

7. Carcinoma in situ is present on the surface at the margin of an invasive lesion provided the general region of the squamo-columnar junction has not been destroyed by the cancer.

8. Similarly prepared histologic sections of in situ and invasive carcinoma show light absorption values of comparable magnitude.

9. The vaginal smears from patients with histologically demonstrable carcinoma in situ are positive in 71% on initial screening and in 80% when the lesion is already known to exist.

Although no one patient has been followed from the earliest morphologic stage of epithelial abnormality of the cervix to the development of undoubted carcinoma, the probable sequence of events based on the innumerable observations of the non-pregnant, pregnant and postpartum cervix suggests that the metaplastic changes of the everted endocervix are the precursor of the atypical squamous epithelium that may ultimately become carcinoma in situ which in turn gradually invades in one or more foci to become true cancer.

ADENOCARCINOMA OF THE ENDOMETRIUM

Evidence that estrogen induced hyperplasia of the endometrium plays a role in the morphologic development of endometrial carcinoma is based upon:

1. Prospective cases, i.e., those which have been followed during the interval in which the endometrium changed from hyperplasia to neoplasia.

2. Retrospective cases, i.e., those in which carcinoma had been proven but in whom prior biopsies were taken months to years before the appearance of carcinoma, and

3. The coincidence of carcinoma and hyperplasia in the same uterus.

The most significant series of prospective cases was that of Corscaden et al who reported 958 patients whose menopause was induced by radiotherapy, 9 of whom developed endometrial carcinoma during an average period of 6.7 years. Six of these patients had had a prior endometrial biopsy and 5 were from the 318 patients (1 in 64 or 1.57%) with hyperplasia whereas only 1 was from the 640 who had no previously demonstrable hyperplasia. Thus the hyperplastic endometrium has 10 times the potential for developing endometrial carcinoma as compared to the non-hyperplastic endometrium. Conversely only about 1.5% of endometrial hyperplasias are potentially malignant. This relationship is epitomized by Speert's statement, "Glandular hyperplasia of the endometrium is a common precursor of carcinoma but carcinoma occurs only in a small proportion of women with endometrial hyperplasia."

The evidence from retrospective cases is based on a total of 70 patients from three series reported by Te Linde et al (22 cases), Speert (16 cases) and the author (32 cases). The intervals during which the endometrium underwent neoplasia varied from a maximum of 25 years in Te Linde's to 13 in the author's series. Various descriptive terms have been applied to the hyperplasias which precede or are associated with carcinoma ranging from those described as atypical, adenomatoid to carcinoid. In the author's series the following terms have been applied; cystic hyperplasia, adenomatous hyperplasia, anaplasia and carcinoma in situ; each type of endometrial change being progressively nearer to actual carcinoma. The histological findings and time relationships in the prior biopsies from 32 patients

who ultimately developed endometrial carcinoma are seen in Table 1. It is clear from these data that all endometria prior to 13 years before the development of carcinoma were negative. Subsequent to that time, however, the endometrium tended to become progressively more abnormal ultimately manifesting itself as carcinoma.

These progressive changes from hyperplasia through anaplasia to carcinoma in situ and invasive carcinoma are seen in the uncommon young patient under 35 (2–4% of all endometrial carcinomas) as well as in the older more typical patient who manifests her carcinoma at an average age of 56. It is significant that Randall finds a 3.5 times greater incidence of endometrial carcinoma in women who have had premenopausal bleeding than in those whose menopause was normal. Such a high incidence of premenopausal bleeding can only be correlated with ovarian dysfunction and endometrial hyperplasia, already histologically implicated in the pathogenesis of endometrial carcinoma.

Additional evidence of the relationship between ovarian dysfunction in the form of feminizing mesenchymal tumors and endometrial carcinoma is seen in the series of 75 such tumors examined by Dr. Mansell and the author at The Free Hospital for Women. In Table 2 it is clear that the more "active" forms of the granulosa-cell theca-cell tumor are twice as apt to produce an abnormal reaction in the endometrium than are "inactive" tumors. Such endometrial abnormalities range from proliferative endometrium (when it should be atrophic) through hyperplasia, anaplasia and carcinoma in situ up to actual invasive cancer. It is significant that 25% of all feminizing mesenchymal ovarian tumors in patients over 50 have an associated endometrial carcinoma. This is approximately eight times the established incidence of double primary cancers (4–5%) and approximately two thousand times the expected incidence of endometrial carcinoma on the basis of pure chance alone.

Some authors, notably Jones and Brewer, believe that hyperplasia plays no role in the pathogenesis of endometrial carcinoma. Their conclusions were based on 68 patients with endometrial carcinoma, 19 of which were premenopausal and 49 of which were postmenopausal. Of the 19, 11 were still menstruating and showed no hyperplasia whereas of the 49 postmenopausal patients, only 2 showed hyperplasia. The author has seen only four patients develop carcinoma while still ovulating and menstruating normally, all of whom had evi-

TABLE 1

Endometrial Findings Prior to Diagnosis of Carcinoma in 32 Patients

Interval Yrs.	Cases Biop.	No. Biop.	Neg. or no Hyperplasia.	Polyp	Hyperplasia			Anaplasia	Carcinoma		
					Infolding	Cystic	Adenom.		In situ	Borderline	Invasive
15–23	6	7	7	0	2	0	0	0	0	0	0
10–13	8	8	0	3	0	6	4	2	1	1	0
6–9	13	18	2	5	2	7	6	4	1	0	0
3–5	10	11	3	2	1	4	7	5	3	1	1
1–2	3	3	0	0	1	0	2	2	1	0	1
Total.....	40*	47†	12	10	6	17	19	13	6	2	2**

* Discrepancy due to patients with multiple biopsies.

† Discrepancy due to multiple biopsies in same time interval.

** Diagnostic errors.

From "Genesis of Endometrial Carcinoma. I. Study of Prior Biopsies." Hertig, A. T. and Sommers, S. C. Cancer **2**: 946–956, 1949.

TABLE 2

RELATIONSHIP OF SUPPOSED ESTROGENIC "ACTIVITY" AND "INACTIVITY" OF 75 FEMINIZING MESENCHYMAL TUMORS AND THEIR ASSOCIATED ENDOMETRIA

Type of endometrium	"Active" tumors		Not "active" tumors		Total	
	No.	%	No.	%	No.	%
Proliferative and min. cystic hyperplasia (postmenopausal)	1	3	3	7	4	5.25
Hyperplasia	6	19	7	16	13	17.25
Anaplasia	6	19	4	9	10	13.25
Carcinoma in situ	5	15	2	5	7	9.25
Carcinoma	8	25	3	7	11	15.00
Total influenced endometrium	26	81	19	44	45	60
Uninfluenced endometrium	6	19	24	56	30	40
All endometrium	32	100	43	100	75	100

From "Granulosa-Theca Cell Tumors and Endometrial Carcinoma. A study of their relationship and a survey of 80 cases." Mansell, H. and Hertig, A. T., Obstetrics and Gynecology, **6:** 385–394, 1955.

dence of some prior hyperplastic abnormality that most observers agree has some intermediary role in the genesis of endometrial carcinoma.

SUMMARY

Although cervical and endometrial carcinoma are quite different in their pathogenesis and general biologic behavior they may have one factor in common; both the endocervical metaplasia which appears to play some role in the initiation of cervical carcinoma and the glandular hyperplasia which often precedes endometrial carcinoma appear to arise as the result of estrogenic stimulation.

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The Use and Abuse of Steroid Therapy in Allergic Disorders[1]

By RICHARD A. KERN, M.D.[2]

THE honor to be chosen to present the first Hira S. Chouké Lecture before this College is all the more appreciated by me because I know there are far more able men in the field to which this Lectureship is dedicated. I am especially grateful to its founder, Dr. Kehar S. Chouké, a Life Fellow of the College, and a former colleague on the faculty of the University of Pennsylvania, who saw fit to suggest me for this honor.

This Lectureship, devoted to the subjects of "*Allergy, Headache and Allied Topics*", was established by Dr. Chouké to perpetuate the memory of his father, Mr. Hira S. Chouké, who in spite of years of suffering from severe headaches, possibly allergic in origin, rose above his affliction to lead a very effective and useful life in his community. He was born in Chouké, a small town founded by his ancestors, in India. Largely self-educated, owing to the early death of his father, he was chiefly interested in farming and in civic affairs. The respect which he soon won and maintained in his own and neighboring towns is shown by the fact that he became head alderman of his district at the age of 22, and that he held this position for the rest of his life. He was gentle in manner, yet courageous in defending the rights of others. Though without formal legal training, his knowledge of the law and his keen intellectual and forensic abilities enabled him to win a number of court litigations, both civil and criminal, even though brilliant attorneys were ranged against him. His kindness, self-sacrifice and public service built him a monument in the hearts of his fellow-men.

His son, Dr. Kehar S. Chouké, was born in Chouké, India, in 1885. He received the degree of Licensed Medical Practitioner (L.M.P.) from the Agra Medical School, India, with honors in 1906, following which he served in the medical department of the Indian Army for seven years. He came to the United States in 1917. After premedical studies at the Universities of Illinois and Michigan, he was graduated in 1922 with honors from the Washington University School of Medicine. For nearly 30 years thereafter he taught anatomy, first at Washington University, then at the University of Colorado (from which he received a Master's degree in Anatomy), and from 1939 to 1951 in the Graduate School of Medicine of the University of Pennsylvania, where he held the rank of Associate Professor. In 1946, he became a naturalized citizen of this country, and in the following year he was elected a Fellow of the College of Physicians of Philadelphia. In a fruitful career of teaching and research, attested by more than 30 published papers and recognized by membership in the principal scientific societies of his field, Dr. Chouké made diligent use of the library of the College. Now in pedagogic retirement, but still serving as a Consultant to a facility of the Veterans Administration, he continues a keen interest in the activities of the College. This Lectureship bears witness to that interest, for which our Fellowship will be thankful through the years to come.

And now to my subject.

Those who in 1949 at the meeting of the Association of American Physicians heard Hench and Kendall (2) describe the effects of cortisone and ACTH in patients with rheumatoid arthritis and acute rheumatic fever, and saw the motion pictures portraying those effects, will never forget that dramatic moment. The great promise which that "Pre-

[1] Hira S. Chouké Lecture I, College of Physicians of Philadelphia, 2 January 1957.

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liminary Report" implied has been abundantly fulfilled in the intervening years. These years have witnessed the development of a group of substances which have brought relief and hope to countless sufferers from a wide range of serious and crippling diseases, while in the hands of scientists they have proved invaluable tools for research.

The more powerful a remedy, the greater is its potential for harmful as well as helpful effects. These effects, both good and bad, will eventually define the limitations of the remedy, and the indications and contraindications for its use. A rapidly growing experience in the hands of many careful observers has now made it possible to formulate a number of rules that underlie a safe and rational use of steroid therapy. Unfortunately, there are also accumulating far too many examples of the unwise use of these substances. Indeed, the abuse of steroid therapy is widespread and its consequences are serious. Of all the diseases amenable to steroid therapy, those due to allergy not only are the most frequent, but they also provide a disproportionately large number of instances of such therapeutic abuse. Therefore it is timely to call attention to the accumulated experience, especially as it reveals the dangers of steroid therapy, and to restate the principles that underly its proper use.

Let me first indulge in a bit of teleological speculation.

Of all man's adversaries, the rat has proved the most capable. (For completeness one might add the staphylococcus.) The rat has chosen to live off the human economy, and if the yearly damage to man's foods and possessions could be accurately assessed, it would prove to be a tremendous levy. The rat has followed man wherever he has gone and has travelled not only in his footsteps but by every new means of conveyance: trains, ships, and planes. The rat has been, and continues to be, the reservoir and vector of a number of man's diseases, be it the plague that marched with the black rat across Europe from the 13th to the 16th centuries and from the crossing of the Bosporus to the crossing of the English Channel, and that probably the Norway rat brought to our west coast at the turn of this century, and so to other wild rodents that now harbor the plague bacillus in at least a dozen western states; or be it the leptospiroses in many places, including Philadelphia and on this very day. Those who have not read the book are urged to read Hans Zinsser's classic of medical and philosophical writing: "*Rats, Lice and History*" (8).

Man is at a disadvantage in his struggle to control the rat. The rat hides himself very efficiently. It has been shown that if 3 or 4 rats are seen about the premises, the census of their colony is 3- or 400. The rat is hard to exterminate by poisons, in spite of its inability to vomit, for the colony is warned by a few foolish tasters, so that the rest shun the bait.

For many reasons, then, the rat has been studied more intensively than has any other creature. Indeed, in several respects more is known about the rat than about man himself. The Wistar rat, propagated in the Wistar Institute here in Philadelphia now for over 250 generations, is the best standardized animal in the world: under given circumstances of diet and environment, one can predict all sorts of data on size, structure and function. The Wistar strain is therefore extensively used in laboratories all over the world, since the information available about it provides an excellent base line in many types of research.

Of all the species of rats, the Norway rat is the undisputed champion. Cunning, resourceful, fierce and predatory, its numbers are limited only by the available food supply. Thanks to its incisor teeth, which in all rodents continue to grow throughout life, it has been known to gnaw its way through one-quarter inch of steel to get food. Ordinary "rat proofing" is a relative term!

For a little over a hundred years the Norway rat has been propagated in the laboratory. However, in no way has it been domesticated: its vicious and aggressive nature commands the wholesome respect of those who must handle it. It occurred to Dr. Richter of Baltimore that 100 years in the history of the rat

would be comparable to 5000 years in human experience, and that the Norway rat in captivity may have undergone changes that have significance in the development of man. Moreover, it is hard to find a group of humans who for 5000 years have had no contact with so-called civilization, while to compare the wild with the "domestic" Norway rat one needs only to set traps just outside the laboratory.

Richter (4) found the "domestic" and the wild strains are as like as peas in a pod in almost every particular, with these very significant exceptions: the anterior pituitary and the adrenal glands of the "domestic" rat were distinctly smaller, the adrenals being about one-third or one-fourth of the size of those of the wild Norway rat, and this reduced size of the adrenal was essentially a matter of less cortex.

Allergists have long known that, whereas the docile guinea pig can easily be sensitized to almost any antigen and can be killed in anaphylactic shock, all rats are hard to sensitize, and to produce anaphylactic shock in a rat one must first remove most of its adrenal tissue. Can it be that man, like the captive Norway rat, has had to fight less and less for his existence, and so has had less and less need for his "fight" and "stress" mechanism, with consequent shrinking in size of his adrenals? Can it be that the meek are inheriting the earth, and with it an increasing vulnerability to allergic disorders, arthritis and a variety of collagen diseases?

The rational use of steroid therapy requires a knowledge of some functions of the pituitary and adrenal glands, and of the behavior of these glands under certain conditions of disease and of unphysiological experience.

Some Functions of the Anterior Lobe of the Pituitary. The pituitary gland plays an important and indeed a dominant role in the endocrine system. It is of course subject to checks and balances by the hypothalamus and this in turn by higher cerebral centers; it is also responsive to feed-backs from other endocrine glands, but the fact remains that in the endocrine system it holds top rank in the chain of command. The anterior lobe produces several hormones, some of which stimulate other glands to perform their functions: the thyrotropic hormone causes the thyroid to secrete thyroxin; the follicle-stimulating hormone and the luteinizing hormone act on the gonads; the adrenocorticotropic hormone (ACTH) reacts upon the adrenal cortex. Partial or complete destruction of the pituitary gland results in symptoms referable to all its target organs. Therefore myxedema, sterility and adrenal failure (Addison's disease, but without pigmentation) are seen in Simmond's disease, Sheehan's syndrome and progeria.

Some Functions of the Adrenal Cortex. The adrenal cortex, in response to stimulation by ACTH from the anterior pituitary, produces at least 28 steroid substances, the functions of only some of which are known with certainty. The outer layer, the *zona glomerulosa*, produces desoxycorticosterone (DOC) and is concerned with salt and water balance. The inner layer the *zona reticulosa*, has to do with gonad function and is the source of estrogen, androgen and progesterone. The middle layer, the *zona fasciculata*, produces hydrocortisone and probably aldosterone, and influences the metabolism of carbohydrates and protein and probably a variety of enzyme systems. *Excessive function* of the cortex (hypercorticism) produces Cushing's syndrome, the clinical picture of which is the same, whether due to a hypersecreting adrenal tumor, or secondary to excessive stimulation by ACTH, endogenous or administered. *Destruction* of the adrenals produces Addison's disease, and this type shows the familiar increased pigmentation of skin and mucous membranes.

Replacement Therapy. Thanks to a long series of researches, including the work of Swingle and Pfiffner and culminating in the discoveries of Hench and Kendall, it is now possible to give satisfactory replacement therapy to patients who have suffered loss of pituitary or adrenals by disease or by operation. In the case of the *anterior lobe of the*

pituitary, such replacement could theoretically be accomplished by giving the several pituitary hormones. In practice this is not often possible since atrophy of the target organs renders any stimulation by these hormones impossible. Even when atrophy has not yet occurred, the pituitary hormones tend to lose their effectiveness through the development of antihormones. Treatment is therefore carried out by giving the hormones of the target organs: the thyroid, gonads and adrenals, as needed. In *Addison's disease*, the therapy depends upon the degree of adrenal destruction, beginning with increased salt intake, then desoxycorticosterone, and, if these fail and there is serious disturbance of nutrition, hydrocortisone.

The basic principle in all endocrine substitution therapy is to give the *least amount of hormone that will restore normal function.* A patient with total thyroid ablation needs ¾ mg. of thyroxin a day—the average normal output of the thyroid. The diabetic is given just enough insulin to cover his carbohydrate intake. Any excess of hormone would produce disease: hyperthryoidism, hyperinsulinism. Substitution therapy for pituitary or adrenal failure is no exception to this principle. While it is not yet possible to predict the extra amount of hormone a patient may need to meet certain stresses, it is now reasonably certain that the normal daily production of ACTH, and therefore the normal basic replacement need, is ¾ to 1 unit per day. Similarly, the daily hydrocortisone quota is from 12.5 to 25 mg.

What has been said thus far disposes of all aspects of substitution therapy. It can be summed up in these words: substitution therapy replaces a hormone that a diseased or destroyed gland is unable to produce, and in an amount never greater than the daily deficit.

The most important corollaries to this statement are: *first*, that in none of the many other disorders in which steroid therapy has had any effect has there been shown to be any deficiency of normal output of ACTH or hydrocortisone: such treatment is in no sense replacement therapy; and *second*, the therapeutic effects of steroid therapy in these many disorders are based upon doses far beyond the amounts of these steroids normally present in the body, and therefore *potentially dangerous.*

Of basic importance in the use of steroid therapy is a knowledge of *the effect of the administration of an endocrine hormone upon the normal endocrine gland of the recipient.* For even the least amount has some effect. The *degree* of effect produced depends upon *how much* hormone is given, and *how long*. If a person is given a small dose of a hormone, his own gland will produce that much less, in order to maintain a normal state. Thus, if a man be given ¼ mg. of thyroxin a day, no thyrotoxicosis results, for his own thyroid will make only ½ mg., instead of the usual ¾ mg. If ¾ mg. be administered the thyroid will not produce any thyroxin. If this is continued for only a week or ten days, no structural change will occur in the thyroid; but if it be prolonged for weeks and months, then an atrophy of disuse will ensue: all this, if only ¾ mg. of thyroxin—the normal daily need of the body for maintaining a normal metabolism, be given.

When ACTH is given to a person, his own anterior lobe promptly produces less than it did. If the dose of ACTH exceeds *1 unit a day* the man's own gland stops making ACTH entirely from the start. For a week or 10 days, this does no obvious harm, but after that, atrophy begins.

If a person receives ACTH, and more than a unit a day, for a long time, say 3 months, then his own *anterior lobe* will have undergone obvious atrophy. During the same time, this excessive stimulus will cause the adrenals to hypertrophy, so that after 3 months they are 3 to 4 times the normal size.

Now if the ACTH be stopped, then the anterior pituitary will slowly resume its function, but even at 6 months after the stopping, *it will not yet have returned to its original size.* At the same time, the adrenal cortex, which now receives only the subnormal stimulus

from its own pituitary monitor, rapidly atrophies, becoming in some weeks only a fraction of its normal size, and 6 months after the ACTH was stopped it has not yet returned to its original size and function.

If a person receives hydrocortisone in a 12 mg. daily dose or more, his own *anterior pituitary* no longer puts out any ACTH, and proceeds after 10 days to undergo atrophy which at three months is of marked degree. At the same time his *adrenal cortex* stops functioning and at the end of three months has shrunken to a third or a quarter of its original size. If now the hydrocortisone is stopped, then the anterior pituitary slowly resumes its function, but 6 months later it is still smaller and less efficient than it was to begin with. The adrenal cortex, after the stopping, slowly resumes its function, in response to the very subnormal ACTH stimulation from its own pituitary, and 6 months after the stoppage, it has not yet regained its original size and function.

In short, a person who has received ACTH or hydrocortisone in the doses mentioned for 3 months has incurred a deficiency of his own pituitary and adrenals that handicaps him for at least 9 months or a year. ACTH and hydrocortisone have been used as examples, but the same holds true for all the substances of the group. A common fallacy is the belief that prednisone and prednisolone do not have this effect, since only 5 mg. daily may be needed to keep a patient comfortable. But a 5-mg. dose of one of these substances is comparable not only in symptomatic effect but in production of glandular atrophy to 20 mg. of hydrocortisone. It is also fallacious to believe that the intermittent use of ACTH completely overcomes adrenal atrophy; pituitary atrophy will only be enhanced.

But what of the effect of very prolonged use: 2 or 3 years, of such therapy? Here there is a dreary succession of disasters in patients, many of whom have been on treatment that long, whether justifiably or not. In these persons the degree of adrenal atrophy can be extreme. Such individuals are in essence man-made cases of Addison's disease. But whereas naturally occuring Addison's disease is a great rarity, there are thousands of cases of *iatrogenic* Addison's disease today. These differ in no way from the natural cases in their great vulnerability to any sudden stress. Any intercurrent infection is a most serious matter, because it can progress with such devastating speed that the patient perishes before help with more steroid and suitable antibiotic medication can be given. Even in hospital and under our very eyes this happens: the arthritic patient dies in 36 hours of a fulminating pneumonia or an acute appendicitis. Or a seemingly minor surgical procedure proves a fatal insult: as in a patient, also an arthritic, who developed a seemingly trifling infection of an olecranon bursa. It was incised in hospital under local anesthesia. After 12 hours the patient felt fine, but in 12 hours more he died in acute adrenal failure. Or the asthmatic patient, subject of a Clinico-Pathologic Conference at the recent Philadelphia meeting of the American College of Physicians, who ran out of her prescription for steroid one day and the next died in hospital in "status asthmaticus", precipitated by a respiratory infection. No one knows just how often these things happen, but they are all too frequent.

With an understanding of the essential endocrine interrelationships in the normal person, and a knowledge of the possible effects of steroid therapy upon the patient himself, one can now examine the *effects which such therapy can produce in the presence of various diseases*. As already mentioned, it is not a matter of substitution therapy. Rather is it a matter of dosage far in excess of normal requirements of steroid hormones. This deserves emphasis. The normal daily output of ACTH by the pituitary is probably not over one unit, yet we give up to 40 units a day. The adrenal glands produce a top amount of 25 mg. of hydrocortisone or less each day, but Rose has used up to 2000 mg. a day in asthma, and Dubois gives as much as 4000 mg. a day

in disseminated lupus. Herein lies the tremendous power of the steroids both for good and for harm.

The effects of steroids can be good or bad. The good effects are essentially of three types: anti-allergic, anti-inflammatory and anti-rheumatic. The bad effects are of many kinds. Fortunately the good effects can be induced rather promptly as a rule, whereas the bad effects are mostly incident to prolonged use. Then it must be remembered that the good effects are purely symptomatic: the steroids cure nothing. If the cause of disease continues to be present, the symptoms will recur promptly when treatment is stopped. Then to obtain continued relief, the treatment must be resumed and continued for longer periods, with the increasing danger of unfavorable effects, to be risked only if threat to life, rarely to comfort alone, warrants. On the other hand, if the cause of disease be no longer present, or of limited duration, or if it be remediable or avoidable, then short-term treatment can be used with safety.

Therefore the indications for steroid therapy resolve themselves primarily into two groups: 1) Those for short-term use, that is, 10 days or less, and 2) Those for long-term use.

Short-term steroid treatment. The indications for short-term treatment will now be cited:

1. Some of the most brilliant results of steroid therapy have been achieved in the treatment of *severe allergic reactions to known and avoidable allergens*. Please note the words *severe, known and avoidable*. Common examples are: *exfoliative dermatitis* from any drug that has been administered; *severe reactions to penicillin and other drugs; serum sickness; severe ivy poisoning* (it could be fatal); *trichinosis* (here the antigen, the protein from dying trichinella larvae, is limited in amount and duration of release); *Loeffler's syndrome* (but not tropical eosinophilia, in which a living, although unknown, agent is the probable cause, since one dose of an arsenical is curative); the *asthmatic who has to undergo an emergency surgical procedure* or a *bronchography while sensitive to the contrast medium; status asthmaticus* (but only when all other measures have been tried and have failed: in the majority of such cases steroids are not necessary). *Malignant neutropenia* is primarily an allergic reaction, but during its course the patient is extremely vulnerable to any pathogens within or around him; therefore steroid therapy must be accompanied by a broad-spectrum antibiotic. The topical application of steroids in the conjunctival sac and the external ear, including post-operative use after fenestration procedures, may be mentioned at this time since some of the indications are local allergic reactions. Such topical use does not involve systemic effects and therefore is harmless. It may require the added use of antibiotics, since infection is a frequent complication.

Topical use within the nose may be helpful to secure pre-operative amelioration in some chronic allergic conditions such as polyposis, or while diagnostic studies are carried out to determine causes, which are then to be avoided or cared for by hyposensitization techniques. The injection of steroids intranasally in allergics must be looked upon as a questionable procedure, since sensitization to the steroid preparation may be so induced, especially in allergic individuals. Hay fever is not a proper indication for either topical or systemic steroid therapy: its proponents have been chiefly those who are inexpert in the specific management of pollinosis or who are unwilling to be so inconvenienced. One should not shoot sparrows with atomic warheads!

Since this presentation deals primarily with the allergic aspects of steroid therapy, other indications for short-term use will be dismissed with brief mention.

2. *Certain acute infections threatening life and caused by known organisms for which there are available effective antibiotics:* Waterhouse-Friderichsen syndrome in meningococcus infection, pneumonia, miliary tuberculosis and tuberculous meningitis, typhoid fever and acute peritonitis are notable examples. Here the combined use of steroid and the proper

antibiotic is life-saving. But it must be remembered that *the antiinflammatory effect of steroids masks the symptoms of infection.* As Salter put it, the steroids prove that it takes two to make a quarrel. The patient under steroids stops to fight his infection with fever and optimal local inflammatory reaction, but the pathogenic organism continues, unopposed, to harm and even to kill. Therefore steroids should never be used in infections for which no antibiotic is available, such as poliomyelitis, or in infections with a prolonged course, such as tuberculosis, leprosy and brucellosis. Malaria is made worse by steroids, and cerebral malaria may be precipitated in those with *P. Falciparum* infection, a type which therefore precludes steroid therapy.

An important aspect of this antiinflammatory effect of steroids on infections is presented by the allergic patient who happens to have a coexisting infection or who may develop an intercurrent infection while on treatment. Examples of the former are sinusitis, bronchitis, and bronchiectasis. Here one must weigh the risk of flaring up the infection and be prepared to meet it with proper therapy. Patients on steroid therapy must be watched for intercurrent infection, and must be warned to report symptoms or significant exposure. Three deaths have recently been reported in children who, while on steroid therapy developed chicken pox that then ran a fulminating course.

3. *A group of diseases and conditions, mostly acute, mostly infectious but of unknown etiology,* have been found to react favorably to the antiinflammatory, and in one instance, the antirheumatic effect of steroids. They include acute rheumatic fever, erythema multiforme, lipoid nephrosis, thrombocytopenic and other purpuras, Bell's palsy, the myelitis following Pasteur treatment to prevent rabies, surgical shock, sprue refractory to other treatment, celiac disease, and as preoperative preparation in adrenal tumor. Gout is not a proper indication for the use of steroids: other measures are safer and more effective.

Before stating the indications for the *long-term use of steroid therapy,* one should consider its *long-term effects.* 1) The *atrophy* of the *anterior pituitary and adrenal glands* has already been mentioned. 2) Since all long-term therapy involves the administration of steroids in excess of normal requirements, there results some degree of *hypercorticism.* To be sure, the full-blown picture of Cushing's syndrome, with moon-face, acne, characteristic obesity, striae, hirsutism, hypertension and disordered gonad function, does not develop overnight, or even at all, if dosage be reduced as indicated. Or it may even be accepted as a justifiable risk under given circumstances. But there are many and less obvious effects of hypercorticism which must be considered and looked for. Since *hypertension* is a threat, the blood pressure must be regularly and frequently noted. *Edema* due to salt and water retention can early be detected by rapid gain in weight. *Mental symptoms* are frequent enough: insomnia, euphoria, at times undue depression that may lead to suicide, changes in personality, and frank psychoses. Psychoses are particularly liable to occur in those who have ever had any previous psychotic trouble: indeed, such people should probably never be given steroid therapy. *Convulsions,* of unknown nature, although cerebral edema has been suspected, can develop suddenly and end fatally. *Glycosuria* is a common effect, that clears up when treatment is stopped. This does not mean that diabetics should not be given steroids, but they will need more insulin while on treatment. It also means that all patients should have regular examinations of the urine for sugar and should curb their carbohydrate intake accordingly. *Osteoporosis,* especially of the vertebrae, may lead to pathological fractures. *Peptic ulcer,* with bleeding and perforation, can occur. That *cleft-palate* can arise in the fetus while the mother is on steroid therapy has been observed in humans and also confirmed in animal experiments. *Allergy* to the steroid is a possibility. ACTH is a good antigen and some degree of sensitivity on second administration after a

few weeks interval has been observed. Indeed, a case of fatal anaphylactic shock has been reported, occurring when an intracutaneous skin test with too large a dose (4 units) was performed because of a history of allergy to ACTH. Fortunately the other steroids are poor antigens, so that reported sensitivities are infrequent, relatively mild, and related rather to parenteral than to oral administration. *Addiction* is a term that is used advisedly in patients who go into a panic at the mere suggestion of reduction or withdrawal of steroid dosage. *All the bad effects* of steroid therapy *occur* with far greater frequency *in those less and less able to cope with them: those over the age of 50*. Some of the bad effects of long-term steroid therapy are due to too high a dosage: the lowest dose that achieves results should be used; others are due to a too rapid withdrawal, resulting in acute adrenal deficiency; withdrawal must be slow, with a step-like reduction of dosage, and a temporary increase during stress or if symptoms develop. For at least a year after the end of prolonged steroid therapy, the patient who is to have an operation should be pretreated with hydrocortisone.

The Contraindications to Steroid Therapy may now be summarized: all acute infections for which there is no available effective antibiotic; chronic infections, notably tuberculosis, leprosy, brucellosis; falciparum malaria; peptic ulcer; diverticulitis; chronic liver disease; severe hypertension; circulatory failure with edema; osteoporosis; severe diabetes; previous psychosis; and, in a relative degree, advanced years. It is unwise to give steroids during pregnancy.

The indications for the long-term use of steroid therapy can be summed up rather briefly as *those diseases for which there is no other help*. The abuse of such therapy results primarily from the fallacious interpretation of the words "*for which there is no other help*." In practice they are changed to "*for which the physician knows nothing else to do*."

In *allergy*, this refers especially to *asthma*. The short-term use of steroids in asthma has already been mentioned in status asthmaticus, when other measures have failed; in asthmatics who need an emergency operation, or who need a bronchography, although sensitive to lipiodol. To this may be added the somewhat longer use of steroid therapy in *severe* asthma, *after* the diagnostic survey has been completed, avoidable allergens have been eliminated and specific therapy may be used for a few weeks until the specific therapy begins to be effective. Finally, there are those cases in which all measures have failed and the patient is a virtual invalid. These have been referred to as cases of "*intractable asthma*." Every allergist of long experience can think back upon a dozen or a score of such cases he has encountered over the years. But this writer looks askance on reports of the effects of steroid therapy in "164 cases of intractable asthma." Far too often, especially in general practice, such treatment is an unjustifiable short-cut around proper diagnosis and specific therapy which a physician is not equipped or trained to perform.

Of course, the patient feels well for a time on steroid therapy, but the relief is so often only temporary. Then when complications ensue, the blame is put upon the "new disease", not upon the treatment which caused it. Or the steroid loses its ability to relieve symptoms and the patient is now referred to an allergist.

Burrage et al. (1) reported an instructive case in point. A patient, aged 60, had developed asthma at 36, and for 24 years had wheezed his way through a rather miserable existence. At 59, in an attack of status asthmaticus, he got relief from a short course of cortisone. At 60, because of continued asthma, and in spite of an earlier history of duodenal ulcer and osteoporosis, he was placed on continued steroid therapy. For 8 months he did well. But 10 months after that he was dead. One might say, "A short life and a gay one." Short, but not gay, for at the end of 8 months the patient suffered pathological fractures of three vertebrae, with painful cord symptoms. Then fol-

lowed 10 miserable months, punctuated by problems of edema, then ulcer recurrence requiring subtotal gastrectomy, and ending in "sudden" death while at stool. The necropsy, in addition to the vertebral fractures and pituitary and adrenal atrophic changes, showed a two-day old, extensive, but asymptomatic and therefore unsuspected and untreated bronchopneumonia.

Nasal polyps can be caused to regress by the topical use of steroids as well as by internal administration. But, as Silcox (5) and others have pointed out, they recur when treatment is stopped, and surgical removal is usually needed, to be followed by proper antiallergic measures. *Perennial allergic rhinitis* is relieved during steroid therapy, but the threat to the patient's adrenals makes unwise the long-term use which such cases would require. Hyperplastic sinusitis, since it has both an infectious and an allergic component, is not helped by steroids.

Severe generalized eczema may force one to the use of steroid therapy. Yet here one is reminded of the difficulties of allergic diagnosis by skin test in older patients. Those difficulties are increased by the effect of steroids in reducing skin reactivity. It is difficult to produce a hive, a skin reaction, in a patient who is also receiving the most potent anti-hive drugs, the steroids. It is not wise to use long-term steroid therapy for eczema in children for fear of serious damage to endocrine development. In eczema the local application of steroids has more justification, although absorption may not be inconsiderable, and in addition there is a possibility of induced sensitization.

Beryllosis can threaten life and so steroid therapy is justified. The same is true of severe *purpura*. *Polyarteritis nodosa*, occurring as it does as often in asthmatics as in all other people put together, strongly suggests an allergic component. Steroid therapy has a beneficial effect, although temporary in most cases. Occasionally, if started soon enough, and if a precipitating allergen such as a drug is known and avoided, it effects a cure.

Apart from allergy, there is a long list of *chronic diseases of unknown cause for which there is no other help* than symptomatic treatment with steroids. Among the *collagen* disorders, *scleroderma* and *dermatomyositis* may show temporary improvement. In *disseminated lupus*, the steroids give very gratifying relief, and may even prolong life a little: certainly they make bearable the remaining months or years of these patients. *Temporal arteritis*, although not a fatal disease, carries the risk of optic atrophy and blindness in half the cases, so that long-term steroid therapy is indicated in all cases.

In ophthalmologic practice, *sympathetic ophthalmia* in a remaining eye thoroughly justifies prolonged steroid therapy to prevent blindness. *Chronic relapsing uveitis* also is amenable to such treatment. *Retinitis with optic atrophy* has regressed from virtual blindness to effective vision as long as one year after the continued use of steroid therapy began.

In the digestive tract, remissions have been induced in *ulcerative colitis*, but here it is best to use the steroids last and for as short a time as possible. *Regional ileitis* has at times been favorably influenced.

Pemphigus, severe *pulmonary involvement in sarcoidosis*, *splenic neutropenia*, *acquired hemolytic anemia* are conditions in which steroid therapy may give more or less relief. Even *acute leukemia* responds for a brief time to such treatment, but neither the outcome nor the duration of illness is changed thereby.

The one non-allergic disease in which steroid therapy is abused as badly as it is in asthma is *rheumatoid arthritis*, and for a similar reason. Whereas the rheumatologist knows much that he can do to ameliorate this disease, and finds it necessary only under special circumstances and only in some patients to have final recourse to steroid therapy, the general practitioner uses the steroids first and alone. It was an example of such therapeutic abuse that prompted me to seek the data that I now present.

Last spring there died in his eighties an old

friend of mine. He had been troubled with rheumatoid arthritis for many years, but managed to get along in spite of it. Then steroid therapy was begun and in due course he died. The circumstances of his death suggested a search of Vital Statistics (7) for a hint as to the frequency of death from steroid therapy.

Figure one shows the total death rate and the death rates for certain age groups in the United States in 1940, 1944, 1949 and 1954. There is a steady fall in each category throughout the period.

Figure two shows the number of deaths in the United States from chronic arthritis (including rheumatoid arthritis), and from rheumatoid arthritis, between 1939 and 1954 inclusive. In addition there are plotted the deaths from chronic arthritis for certain age groups as well. (This was done because no figures for rheumatoid arthritis by age groups were available.) The curves are not drawn continuously, because in 1949 the sixth decennial revision of the list of causes of death was put into effect, so that figures before and after that date are not exactly comparable. In the same year, 1949, steroid therapy was introduced.

In the upper left hand side, before 1949, it will be seen that the incidence of *chronic arthritis* shows a rather level course: only in those in the seventies and the eighties is there an upward trend. *Rheumatoid arthritis*, on the other hand during this same presteroid era shows a steady upward trend, with a death rate of 0.2 per 100,000 of population in 1939 and 0.3 in 1948.

After 1949, the number of *chronic arthritis* deaths is no higher, except for high points in

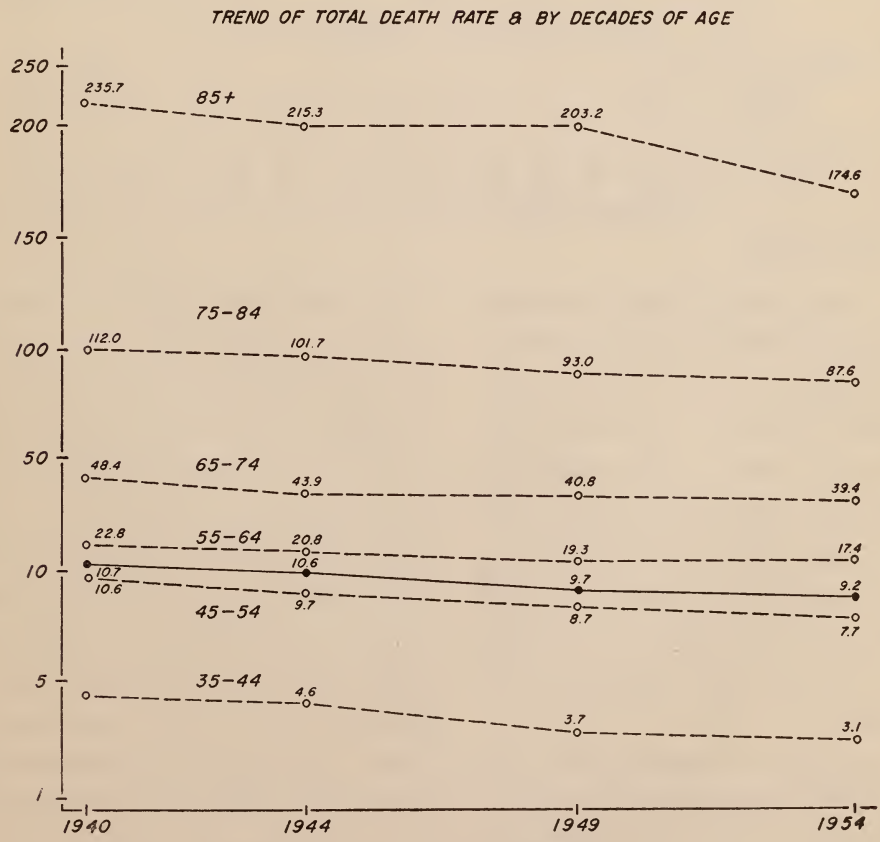

FIG. 1. Note: Death Rates per 1000 population.

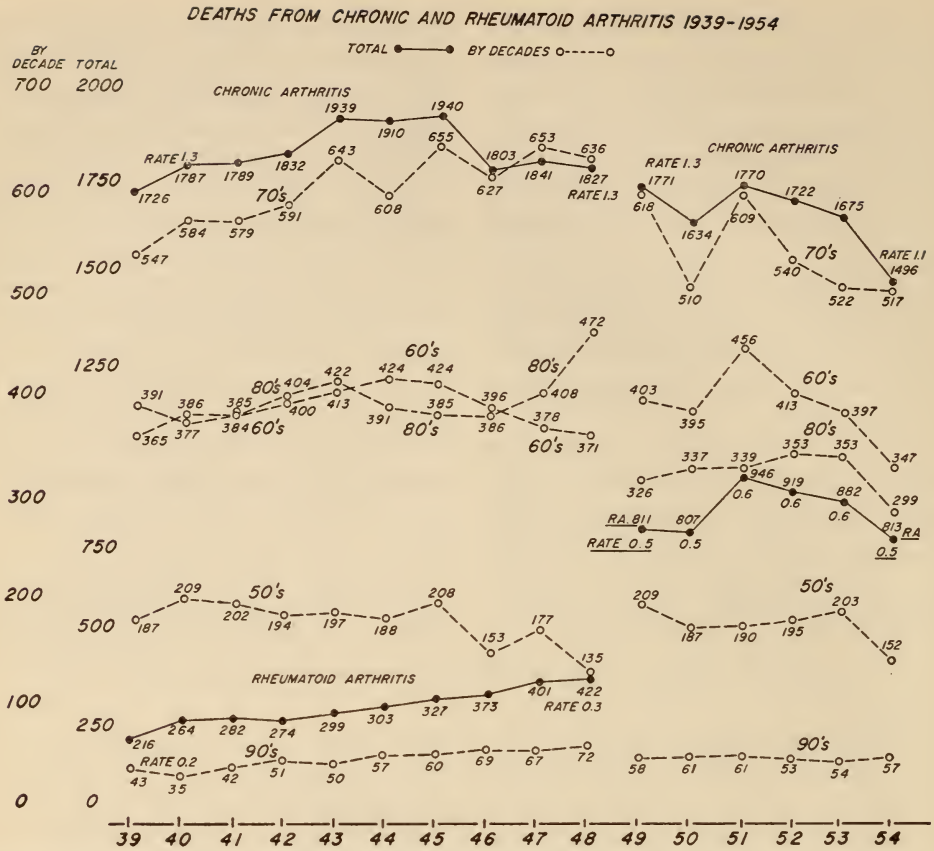

FIG. 2. Note: Death Rates per 100,000 of population. The Solid Line is the total death rate. Broken lines refer to age groups by decades.

1949 and 1951, and then there is a decline in total cases, and a fall in rate from a high of 1.5 in 1945 and 1.3 in 1949 to 1.1 in 1954. *Rheumatoid arthritis*, however, shows a definite peak in 1951, and the death rate that year was 0.6. However, I repeat that figures after 1949 are not exactly comparable with those before because of the change in nomenclature. All that one can say, then, is that there is no significant change in the mortality of chronic arthritis, if anything a slight recent decline, while that from rheumatoid arthritis, which was rising slowly before 1949, has not continued to rise.

Now to return to my deceased friend. I told you he had had rheumatoid arthritis. But that was not the cause of death which appeared on his death certificate: that said "duodenal ulcer".

Figure three shows the data for deaths from *peptic ulcer*. Before 1949, there is a definite downward trend in the total number of deaths from ulcer; the downward trend of deaths in those under 60 more than offsets the upward trend in those over 60, especially in the sixties and seventies. After 1949 there is a steady increase each year in the total deaths, for although deaths in those under 50 have continued to fall, there is an increase in the fifties as well as in all groups over 60, especially again in the sixties and seventies. In this graph there is one curve that is drawn as a continuous line, because government statisticians have figured out a corrected rate for deaths before 1949 that is comparable with those after that. There is also a curve for uncorrected rates before 1949 in a broken line. It will be noted that the newer computation

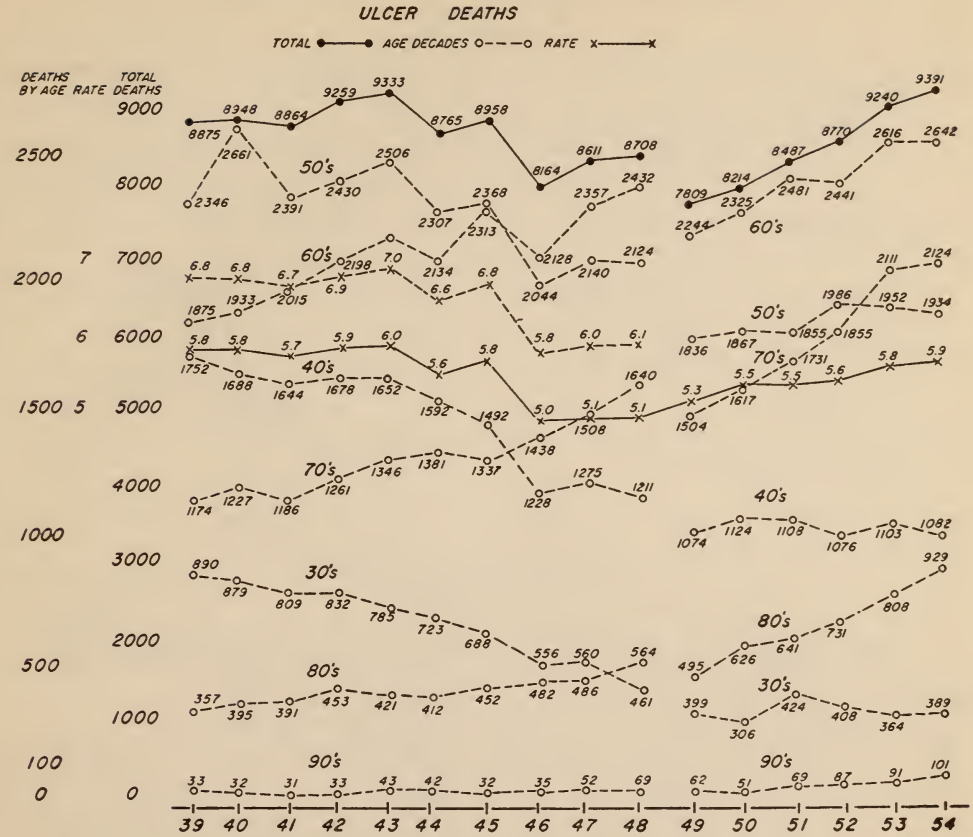

FIG. 3. Note: Death Rates per 100,000 of population.

gives lower rates for the earlier period, so that the increases after 1949 are the more significant.

All of this still proves nothing, even though the increase of ulcer deaths in the fifties and the undue increase in the sixties are suggestive of a new cause or new causes operative in the production of ulcer. Thus, during war time, ulcer and ulcer deaths increase (the peak was in 1943), but it is the old who are more likely to succumb. After all, the old must die of something, and since deaths from infections are fewer, there will be an increased mortality from other causes. But this is certain: ulcer is increasingly more dangerous in the aged, therefore a potential cause of ulcer, steroid therapy, must not be used lightly in those over 50.

The data for deaths from asthma are more revealing (Fig. 4). Before 1949, there is a slight upward trend in total deaths, notably in those over the age of 60. The death rate at the end of this earlier period is also slightly higher, 1.8, as compared with 1.6 at the beginning, but lower than the peak 2.0 in 1943 and 1944. These earlier death rates are plotted in a broken line. The National Office of Vital Statistics (7) points out that to compare the mortality figures for asthma before 1949 with those after 1948, the former must be multiplied by a factor of 1.6. Therefore a second set of death rate figures has been so determined and these are plotted as the one solid line that runs *continuously* through the graph.

The figures on deaths under age 30 (left upper quadrant) show no significant change before or after 1949. But after 1949 there is a sharp upswing at all ages over 40, with a peak in 1952 for all ages except those over 90, whose peak was reached a year earlier. This definitely

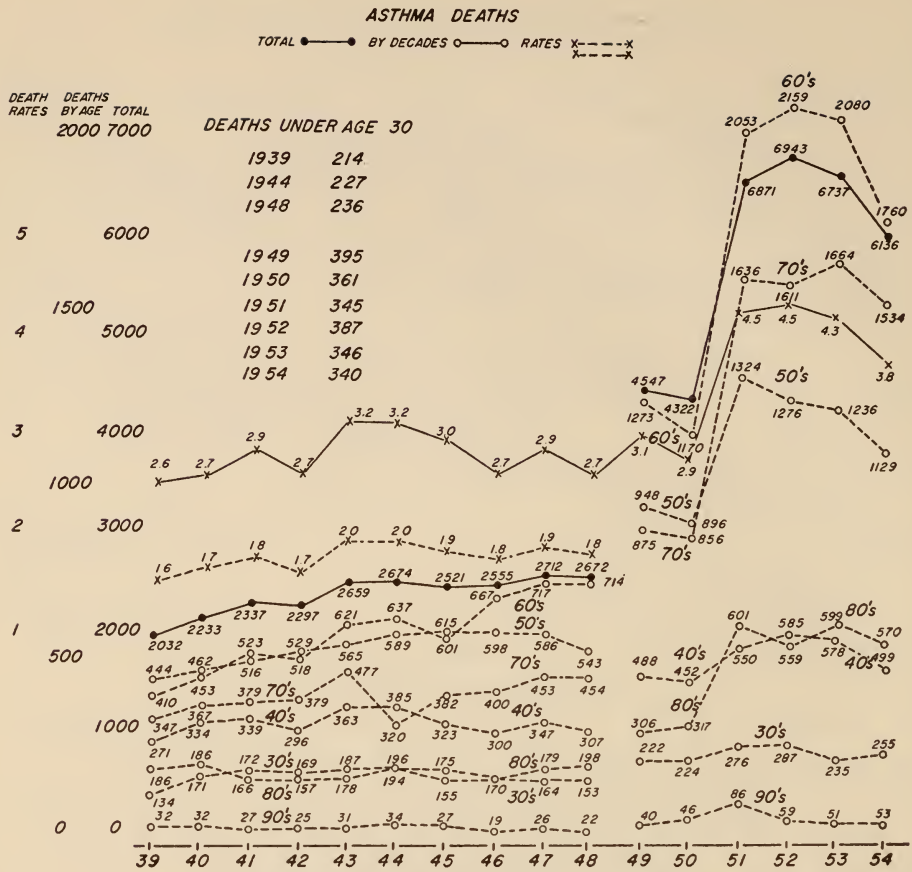

FIG. 4. Note: Death Rates per 100,000 of population. After the presentation of this lecture word was received from the National Office of Vital Statistics (7) that to compare figures for asthma before 1949 with later ones, it is necessary to multiply the earlier figures by a factor of 1.6. The solid line which runs *continuously* through the graph plots the death rate figures which have been so calculated.

suggests that in this period we seem to have eliminated a goodly share of our "intractable" asthmatics by means of steroid therapy. But the number of deaths from asthma and the death rate is still 25% higher in 1954 than in 1949 or in all of the period before 1949.

Final proof of the dangers of steroid therapy is unfortunately not to be obtained in vital statistics. No deaths are listed as due to steroids. Doctors' mistakes are still buried, not reported.

The death rates by age groups for all three conditions: chronic arthritis, asthma, and ulcer, are combined in Table 1. Although the figures before and after 1949 are not directly comparable, certain trends may be significant. There appears to be a definite decline in deaths due to chronic arthritis. But this may be more apparent than real, since some of the increase in ulcer deaths in older persons may represent the results of steroid therapy of arthritis. The increased death rate in older asthmatics seems clearly to implicate such treatment. Prolonged steroid therapy in arthritics and asthmatics over 50 should not be undertaken except upon truly urgent indications. The high and rising death rates from asthma and from ulcer in those over 60 (italicized figures) call for serious consideration by all physicians.

In October, 1956, Hiddlestone (3) stressed to New Zealand physicians the growing importance of asthma, and cited the rising number of

TABLE 1

CERTAIN DEATH RATES PER 100,000 POPULATION BY AGE GROUPS IN 1940, 1944, 1949 AND 1954

Chronic Arthritis					Asthma				Ulcer				
Age	1940	1944	1949	1954	1940	1944	1949	1954	Age	1940	1944	1949	1954
20's	<0.2	0.1	<0.1	<0.1	0.4	0.4	0.5	0.5					
30's	0.3	0.24	0.16	0.1	0.8	1.0	1.0	1.1	25–34	2.3	2.0	0.9	0.8
									35–44	5.9	5.1	3.5	3.2
40's	0.5	0.5	0.4	0.3	2.0	2.2	2.5	2.4					
									45–54	11.6	10.2	8.4	8.1
50's	1.5	1.4	1.4	0.9	3.6	4.3	6.3	6.9					
									55–64	17.6	18.4	16.3	15.9
60's	4.5	4.7	2.7	2.9	5.4	7.0	12.9	*14.9*					
									65–74	22.2	22.0	25.3	*28.1*
70's	13.6	12.3	10.7	7.8	8.5	6.5	15.3	*23.6*					
									75–84	29.6	23.7	31.6	*42.2*
80's	29.7	24.4	18.1	10.3	14.3	12.2	17.0	*19.6*					
									85+	27.9	—	37.3	*51.8*
90's	—	—	—	—	—	—	—	—					

TABLE 2

TOTAL DEATHS AND DEATH RATES FOR ASTHMA IN NEW ZEALAND (HIDDLESTONE)

Year:	'39	'40	'41	'42	'43	'44	'45	'46	'47	'48	'49	'50	'51	'52	'53	'54
Deaths	28	24	35	47	39	35	53	30	54	44	58	140	159	208	179	139
Rate (per 100,000 population)	1.71	1.46	2.14	2.86	2.38	2.11	3.12	1.70	2.99	2.38	*3.08*	*7.28*	*8.16*	*10.42*	*8.73*	*6.63*

deaths from this cause and the death rates. The figures are strikingly similar to our own, with a sharp increase after 1949, a peak in 1952 and a slight fall-off thereafter. Moreover, the age group pattern in the year 1952 shows that of the total of 208 deaths, 61 occurred in the sixties, 50 in the seventies, 40 in the fifties, and 21 in the forties, again as with use, maximal in the sixties. He was, however, not concerned with any possible unfavorable effect of steroids. Indeed, he pointed out that infection plays a dominant role in death from status asthmaticus and advises 24 hours' treatment with antibiotics and then the additional use of cortisone or hydrocortisone.

A final word about the newer steroids, *prednisone* and *prednisolone*. Much has been written about the advantages which these substances have in certain respects over other steroids. I will refer to only one excellent article by Spies, García, Díaz, López, Reboredo and Suárez (6) which appeared in October, 1955, in the *Journal of the American Medical Association*. On the basis of a large number of patients with various diseases treated with these substances, the authors conclude that they possess the same antiallergic, anti-inflammatory and antirheumatic properties as cortisone and hydrocortisone, and, in addition, they do not cause retention of sodium and water. The latter quality permits their use in patients with circulatory conditions in which any fluid retention would be seriously embarrassing. But they emphasized that these drugs produced the same side effects and in the same frequence with therapeutically effective doses as do cortisone and hydrocortisone. Indeed, they cautioned that patients on these drugs must be watched more closely, since damage could ensue more insidiously in the absence of the red flag of edema. They also counseled that these drugs be used intermittently rather than

continuously, and that other measures be used to the utmost of their effectiveness in preference to the steroids.

What happened to this good advice?

Every one who publishes an article in a medical journal wonders what his readers think of it. He can gauge its value in some degree by the requests for reprints which he receives. But he is sure the article is good if one of the journals distributed gratuitously to all physicians (the advertisements pay the cost) selects the article for republication in abstract. And so in January of 1956 "*Medicine*" published a very good resumé of the article by Spies and his colleagues under the title, "Therapy with Recent Corticosteroids."

But you have really arrived if your paper gaind the attention of *Readers Digest*! So in December, 1955, this paper received high approval in an article by DeKruif. Furthermore, the foreign-language editions of that publication also took it up. As I read the Spanish edition, I encountered it in the March number of *Selecciones del Readers Digest*, but with this title: *Superaspirina para los Artríticos:* superaspirin for arthritics.

Little wonder that there is an increasing tendency for general practitioners to treat their patients with asthma or arthritis or hay fever with these drugs and without proper diagnosis or careful follow-up. When treatment fails or complications arise, the patient is turned over to the specialist. But what of the damage that has been done in the meantime?

Some people do worry about them. Now I quote from a letter which Armour Laboratories sent early in 1956 to all physicians:

"Dear Doctor:

'Prednisone and prednisolone were originally introduced as safer, more potent analogues of cortisone and hydrocortisone. The promise of greater safety was responsible for the enthusiastic acceptance of the new steroids and has led to a remarkable increase in the number of steroid users. While the new steroids are a valuable therapeutic addition, our concern deals with a false sense of security which appears to prevail among physicians who had previously shied away from corticoid therapy.

"It appears to us from surveys that a great many physicians evaluate safety in steroid therapy essentially in terms of side actions, such as sodium retention and weight gain, hypertensive effects, decrease in sugar tolerance, moonface, etc. Yet these side actions hardly deserve being called dangerous because of their gradual, readily noticeable appearance and their reversibility on dosage reduction or hormone withdrawal. Indeed, these side effects, particularly weight gain, are really early warning signals of beginning overdosage.

"One effect, however, adrenal cortical suppression and atrophy, is not an overdosage effect, but the unavoidable accompaniment of any corticoid therapy, whether cortisone, hydrocortisone, prednisone or prednisolone is employed.

"What appears to be ignored are these three facts: 1) that the new steroids, because they are more potent, are also more potent in inducing side effects and adrenal cortical atrophy; 2) that therapeutically equivalent doses of old and new steroids have the same undesirable effects, . . . 3) that absence of water and sodium retention implies a greater rather than a lessened risk of exposing the patient to the various other side effects."

Nevertheless other drug manufacturers are compounding the felony by purveying preparations containing steroids and aspirin and antihistaminics. Indeed some are applying for permits to sell steroids over the drug store counter without prescription, and that, of course, means without diagnosis or medical supervision.

There is the story. It contains food for thought for all physicians, for sooner or later most of them must come to grips with the problems it presents. Their solution involves, first, a knowledge and understanding of the indications for steroid therapy, of the other

therapeutic measures that must be tried in various diseases *before* resorting to steroid therapy, and of the side effects and dangers that such therapy may entail; and second, the wisdom to decide when to take those calculated risks. But above and beyond these considerations lies an ethical principle: *Primum non nocere*. What was enjoined in the Hippocratic oath is binding upon the physician today: that he shall not knowingly do his patient any harm.

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Prolonged Illness—The Reorganization of Home and Hospital to Meet the Problem[1]

By E. M. BLUESTONE M.D.[2]

BEFORE proceeding with the elaboration of my thesis, I respectfully invoke the spirit of Professor James M. Anders, the scholar, teacher, and pioneer in health and medical care, who entered this life more than one hundred years ago and enriched the lives of countless others not only in his own time, but in generations yet to come. The form of homage which my late friend Professor Hobart A. Hare prescribed to the memory of this great humanitarian through this lectureship is a richly deserved immortality. I firmly believe that the argument which follows would meet with Dr. Anders' generous endorsement since it embodies much of his own teachings on behalf of humanity.

The semantics of my subject is of unusual importance and demands a priority on the attention of the student of medical practice. It is, in fact, the first of a series of numerous obstacles which confront and confuse the planner of medical care. Men who evade reality have hidden behind artificially slanted definitions, or those which lend themselves to easy misinterpretation; have leaned on them for support and, wittingly or unwittingly, have permitted them to mislead us into the belief that they are unchangeable, helpful (if only in a negative way) and accurately descriptive. The fact is that new designations for old problems, as well as for their ingredients and premises, must now be elaborated, to correspond to the truth however distasteful it may be, to dispel the fog in which they are enveloped, and to conform with new aspects, attitudes and requirements. Above all they must enable us to speak the same language and to understand each other. The ultimate purpose is to bring clarity to the picture of medical care at the outset, in the face of the most difficult and most persistent problem known to the human family. Since prolonged illness is the last great question which the practice of medicine and the allied sciences, working together in the closest harmony, will be called upon to answer, it is all the more important to know what we are striving for and to give it an applicable helpful and honorable name.

The control, if not the conquest, of the infectious diseases is only one aspect of the victory of the eternal urge to prolong life while making it useful, comfortable, and at least endurable. As such victories accumulate and their fruits are placed at our disposal, how shall we adjust our plan of organization for medical care, as well as social care, during periods of curable or incurable chronicity in such a way as to encourage further victories? The method is less redoubtable than prevailing circumscribed hospital policy would lead us to believe, if we will but accept the inevitable doctrine of ultimate limitations and refrain from applying it in temporal terms of restraint. Preventive medicine does, of course, contribute its share in the attempt to delay the final accounting. The prospect of death does not deflect its course. The protean spirit of charity flowing from the strong to the weak, which supplements and helps give meaning to the work of the physician and sanitarian, also contributes its share. In its elemental form, however, the problem of chronicity is deeper and broader than this. What then is chronicity and how shall we redefine it in terms of the

[1] James M. Anders Lecture XXXVI, College of Physicians of Philadelphia, 6 March 1957.

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realities and requirements of prolonged illness? What does it profit us to judge the effect of disease on society as if duration of illness were a punishable offense? Continued search for the ideal or its approximation is encouraged by a clearly written preliminary protocol of any experiment. Let us therefore state the premises and conclusions in words that we can all understand. These relate to the various phases of health and sickness—to hospital and to home—while there is life left that must be sustained.

In the pre-scientific era of resignation, hopelessness, and incurability, men spoke of "chronic disease" as of something final, like a sentence of death which must be executed at some far-off day without benefit of appeal. They had little or nothing to offer such patients but prayer—and custodial care (food and shelter) accompanied by such sporadic medical visits as may have been available in that era and could be spared, if they could have been commanded, after the needs of the responsive or unresponsive acutely sick patient had been met. Special institutions were created and maintained after a fashion, independently, thru the brave efforts of a higher quality of philanthropy moved by social urgency. This happened when the chronic guest was no longer wanted or desired elsewhere, either because he could not sustain the interest of his medical attendant or pay for it, or because the unrelieved burden was more than his unsubsidized family could bear. Chronic disease was looked upon in earlier days as a curse of God.

This serious split in hospital organization denied to the "chronic" patient his only chance for recovery, weak though it may have been. It was a division of labor based on false premises. Poverty had much to do with the case, far more than it does today in an era of social security. The patient who could not finance his own care was literally in a vicious circle, in which poverty and so-called chronic disease invited each other and then kept company distressingly, until death supervened after an intolerable period of time. Doctor and social worker stood by helplessly, or found themselves too busy with more promising clients elsewhere who were in possession of both clinical and financial currency, while a small band of scientists and humanitarians sought ways of breaking the circle by constant probing for some weak medical or social spot, or both. We can find no better illustration of the close and vital interrelationship between medical practice and social service than this, in which improvement of one aspect of the case is followed by improvement in the other. Better preventive, diagnostic, therapeutic, and rehabilitational care means a more productive and self-sustaining patient for a longer period of time. Better social care, in which the enemies lurking in a man's environment are identified, held in check, and nullified, means a healthier and more comfortable client.

"Chronic" disease of the earlier period was so identified because of the time element in its duration. In the absence of anything but palliative medical activity social activity saw to it that the patient was kept out of the cold till God in His own good time could receive him. The "chronic" patient thus became synonymous for a long period of time with the nondescript "custodial" patient, an invidious designation even though it harbored the smoldering ashes of a later flame. The method of choice in the care of this type of patient was the product of helplessness ("Hobson's choice", as many thought). Our forefathers relied heavily on the factor of distance to free their time, energy, and money, for the benefit of the luckier ones who were able to gratify all sides by responding more quickly to medical effort. Not being able to solve the problem of the "chronic" patient in any but a passive way, and lacking the equipment to enter and explore areas that were so dark, they transferred him to distant points where, in his rustication, time could have its way with him. The dawn has now arrived and the light that is streaming in is beginning to illuminate the prolonged phase of illness. The result is that we have a revised goal to strive for and one that is worthy of modern medical progress.

During the thirties we transformed the poorly-defined "chronic" patient (any patient who was not "acute") into a better-defined "long-term" patient. However, illness being illness, the only difference between its short-term and long-term phases continued to lie in the challenge of the latter as compared with our success with the former—which was due, in turn, to the persistence of someone with a prolonged problem in medical care! Time marched on and the last decade has produced the kindest designation thus far, one which looks upon and deals with "prolonged illness" as, literally, a prolongation of the signs and symptoms of the acute phase beyond the period of agonizing manifestations. We are not yet, and probably never will be, in a position to tell at what point a dividing line may be drawn beyond which a man may be abandoned to his fate.

We thus have a helpful, less severe, and more encouraging definition to guide us in our planning. With the broadening and intensification of laboratory effort, we are in a better position to change our attitudes, and consequent budget allocations, in positive terms of need rather than in negative terms of duration of illness. I need not illustrate here, in a period of medical history when huge sums are being offered to encourage persistent effort with persistent illness. During our time government has joined hands with philanthropy in the subsidy of medical research to increase the tempo of activity with prolonged illness. Organized medical care is thus being challenged to keep pace, to plan the required facilities in the laboratory and elsewhere, in home and in hospital, and to pursue the matter relentlessly.

By contrast, we can now look at the case of the paradoxically fortunate acutely sick person who commands a relatively quick and mostly adequate response. He requires more medically than socially and gets it not only as a normal response to the call of mutual aid in urgent circumstances, but because remedies, are, statistically speaking, more frequently at hand, the duration of the illness is short, and the results often dramatic, or at least rewarding, to the medical attendant. The patient is most often young and has strong natural powers of resistance, of survival, and recuperation. The problem in medical recruitment becomes aggravated when his signs and symptoms become dulled and persistent over a longer period of time. Fortunately for the borderline case between acute and chronic every new achievement in medical practice helps to keep him on the right side. The doctor is provided more and more with the tools of productive work, the time, and the space in which to work, the wherewithal needed for successful work—and the encouragement radiating from those in authority, who represent community effort in medical care. We are, in fact, looking forward to the day when prolonged illness will be treated as an acute problem for reorganizational purposes.

We see therefore that the definition of a hospital depends on environmental factors that happen to be active and influential in different periods of time. In the beginning, the hospital was a primitive form of communal housing in which the unclassified sick were transferred out of their inadequate homes and kept while their neighbors were shielded from contact with their illnesses (a reminder that good housing is closely related to the subject of hospitalization in any community). During a long period of years this kind of hospital dictated its definition. The medical response was poor because the doctor arrived at the bedside almost empty-handed and came away too often disappointed, unlike his modern counterpart who is blessed with an impressive diagnostic and therapeutic armamentarium for routine as well as research purposes.

During our own generation the tempo of change has increased with breathless speed. Those of us who participated in the adjustment of the early hospitals of this century to the requirements of bacteriology, radiology and surgery, to give only a few examples, are almost overawed by the most recent demands for adjustment on a much wider front. In terms

of money we are spending an eloquent $24 a day per patient in the voluntary "acute" general hospitals of New York City and this average figure will not stand still. It reflects greater activity in all directions (though it does not yet purchase better non-professional service) with one possible exception, and that is in the area of prolonged illness. It must be said at once, however, that more and more hospitals are increasing their interest in this aspect of medical care and are moving toward its absorption into the hospital complex at least functionally, and sometimes structurally. Community interest is being stimulated and applied as a wholesome pressure on hospitals and this is due not only to the increasing requirements of an older population, but also to the new modalities of medical care which the science of medicine is steadily placing in our hands for ready use.

We now see greater hesitancy in making a final prognosis of incurability as an excuse for inaction, and a greater recognition of the thought that we may be misled by such fateful judgments. Others, with greater knowledge insight and creativeness, may be standing by to prove us wrong. We are beginning to accept the fact, which was ignored or suppressed in earlier years, that hospitals must not be created for curable patients only. As a result the line of demarcation between "acute" and "chronic" is moved forward while medical knowledge accumulates and further opportunities for continued progress are grasped. The same specialist deals with "acute" and "chronic" phases of the same categories of "curable" or "incurable" illness during the course of his work. There are no separate specialities for either phase of illness.

There have been many instances in which one doctor has succeeded where another failed—a fruitful source of gossip among medical men! One hospital may succeed where another fails. The result is that hospitals are constrained to make a wider search for remedies all the time, as well as for the staff that is required to discover and apply them successfully. Helpful governmental as well as philanthropic subsidies to hospitals are increasing and so are third-party payments, best exemplified by pre-paid insurance for medical care under as many circumstances of illness as possible. We seldom hear of financial bankruptcy in a voluntary community hospital, though temporary insolvency is still too common. Furthermore, we are now beginning to emerge from another kind of insolvency—a clinical deficit which has dogged our steps over the years.

Medical interest in hospitals will be sustained and stimulated increasingly as instruments of precision and the other tools of diagnosis and therapy, including the space to house them and the personnel to use them productively, are made available. This means that, in those fortunate locations where such provisions are made, the medical staff need no longer enter the arena against an implacable foe with nothing but bare fists to use in defense of its patients. There is gradually emerging, though not yet keeping pace with the advance of medical science, a type of hospital which will either reorganize so as to retain somewhere within its curtilage and for a longer period of time, those patients who suffer from prolonged illness, or accept medical jurisdiction for their continued care off the grounds. The tendency of society to concentrate all that is best in the general hospital continues gratifyingly and we find in this establishment the best that a community can offer in medical care at any time in any place. In passing it must however be recorded that the rank and file of the practicing medical profession which surrounds and nourishes the hospital is still at arm's length from it in too many cities. We should find its position closer to its center than to its periphery.

It is clear from all that I am saying here that an institution which commands the best in medical care in any community should be available to any patient who needs it, and to his family physician whenever doubt arises as to the best procedure to adopt in diagnosis or therapy either because of lack of skill or lack

of money. Furthermore, what is readily available to the patient inside of the hospital, with or without payment, should be as readily available to a patient outside of the hospital who may not require the use of an expensive hospital bed, and on the same terms. These prime facilities should also be readily available to a discharged or transferred patient whose need for such facilities, however less frequent or intensive, should be of continuing concern to the hospital as "unfinished business". We hope to see less and less of the earlier tendency to isolate, segregate, or rusticate a patient during a period of continuing medical need when persistent search might produce the desired remedy. Distance has a way of alienating the problem while reducing the trauma to the conscience of hospital trustees. Where the patient's plight is deliberately aggravated by the handicap of distance and the scarcity of medical facilities (space staff and equipment) he remains a constant reproach to the vaunted ideals of the general hospitals.

What we shall see as a logical consequence of medical progress is the redistribution of medical help in accordance with need and not in obedience to artificial standards of eligibility for admission or retention applied in the admitting room arbitrarily, or on the wards impatiently and often unsympathetically. When this kind of reorganization will come into its own—and there are welcome signs of it that are increasing daily—patients who still require a hospital bed will get it at any point in time and space when they need it, and for as long a time as they need it. The corollary to this proposition will also be true—no one will occupy a hospital bed a moment longer than he needs it.

Distance is significant in urban as well as rural areas. In actual practice, distance in relation to medical care should be inversely proportionate to medical urgency. The longer it takes to apply medical care when it is needed, the greater the threat to life and comfort and this holds in all phases of illness no matter where it manifests itself. Time waits for no physician. Delays may not only be fatal, they may make the difference between acuteness and chronicity, between comfort and discomfort. Obviously, therefore, distance must be reduced and every facility offered either on the premises or in portable form to provide a patient with an adequate response, no matter where he is located.

What I am saying here is that the crowded, or overcrowded, general hospital must not be duplicated elsewhere (at considerable unnecessary expense) in order to provide needed hospital beds for the independent management and study of chronicity. By every rule of logic the problem must be solved, or at least met squarely, by the addition of beds in one location, where the required facilities will be available immediately for less frequent as well as for more frequent application. I repeat that the same specialty deals with the "acute" and "chronic" phase of any category of illness. The structural problem imposed by such a requirement is readily assimilated by the profession of architecture, and particularly so if a sound functional program of continuous medical care is placed in its hands.

We come now to the region beyond the walls of the hospital where the home, and the family from which the patient derives, are to be found. If we read the lessons of modern Social Medicine correctly, we cannot separate them for study independent of the environment which surrounds them. We may remove the patient temporarily or permanently from his home but this home is nevertheless the immediate shelter which has given him a roof over his head, privacy, protection and a place to receive his friends without doing violence to the comparable rights of sick neighbors. The air which he breathed, the climate and the weather surrounding his home, may have affected him in health and in illness. Everything in his neighborhood, without exception, may have influenced his status with respect to his home, his personal background and his relationships. Therefore when he takes sick, either because of injury, deformity, inflam-

mation, or new growth, there is enough quantitative and qualitative causation in his environment to command the attention of physician as well as social worker. I have referred elsewhere to the environment of a sick man as a gigantic culture medium in which mischievous pathogens may flourish, depending on the weakness or strength of his natural and acquired protective mechanisms.* The psychosomatic approach to the patient during illness must be supplemented by the environmental approach so that mind and body can be studied together as part of the environment in which life must be lived. Viewed from this angle, the home and the hospital assume a vital and indispensable relationship to each other.

The home must sometimes become a personal and highly individualized hospital for the patient, and the reverse is also true—the highly technical impersonal hospital must be converted into a temporary home for the sick man. The prevailing barriers to reorganization—negativism, vested interests, inertia, fear of the loss of institutional identity and appeal—in putting such principles into practice in every case are known to us but they can be surmounted. If the patient's needs are borne in mind, the two resources—home and hospital—can become interchangeable as occasion demands, and complementary on the most favorable terms. This at least is the ideal of medical care and it is therefore the gravamen of the organizational problem. It thus becomes clear that we need (a) hospitals with a more humane i.e., more individualized and expanded orientation, as well as (b) better housing both for preventive and rehabilitational purposes. I must remind you at this point that the goal of rehabilitation goes beyond medical cure and is only reached when the patient is restored to his environment under the most favorable conditions for him.

When integration of effort on behalf of "acute" and "chronic" will be accomplished, based on the necessity for unbroken continuity of care, and also during the intervening period of organizational transition, the question will arise as to the disposition of a patient who is ineligible for admission (or of retention after admission) to a hospital, and does not require intensive hospital care during his illness. Poverty is a social disease more than a strictly medical disease which does not by itself qualify a patient for admission to a hospital. Under such circumstances we must consider the possibility of making available hospital services and resources to extra-mural as well as intra-mural locations. In any case, where a patient does not require a hospital bed for medical surgical or specialty purposes, he and his family physician should be subsidized, if necessary, by the hospital to the extent of its ability, with the understanding that the home bed which is situated extra-murally will have the same expert supervision as the hospital bed which is situated intra-murally. There will be a difference in the intensity of activity, but medical opportunity will remain.

Criteria for medical care on both sides of the hospital wall are easily established under such a division of hospital labor. Experiment has proved successfully that integration of hospital effort ("acute" and "chronic", intra-mural and extra-mural, in-patient and out-patient) is the nearest kind of assurance of continuous care, serving doctor and social worker as well as patient within a world that must forever remain incomplete. That such a plan of medical care requires adjustments on both sides of the hospital walls is clear, but these are by no means formidable. In the case of the home, relatively less expensive subsidies of various kinds may be necessary to make it satisfactory for the application of extra-mural hospital care. In this case the patient can be nursed by his family, with some outside professional help, and have the feeling that he is benefiting from a highly concentrated medical effort which is superior, and neither diluted nor dissipated by neighbors in a ward who might be more or less sick than he is and who are compelled to share

* Bluestone, E. M.: "René Sand—In Memoriam", Hospital Management **81:** 58–60, February, 1956.

the precious time of the doctors with him. In case of the hospital, a comminution of the open ward principle of hospitalization—literally, its pulverization—to make individualized service more possible is required. The fundamentals of Home Care have been described and explained in the literature and need not be labored here.* As a program its acceptance has been almost as universal as it has been helpful. It remains only to add that the relationship of the home to the hospital should be direct, and not indirect (or delayed) as in the case when a middleman-agency takes over, only to be compelled to act as purveyor of borrowed medical care at a later date when hospitalization may be needed.

Such a reorganization of home and hospital (and I hope that I have not been assigned too strong a term, and too forbidding, to describe the case) can be carried out with relatively slight additional expense, at far less than the combined cost of additional beds in the hospital for construction and maintenance. The total subsidy of the home which may be required (by the community acting thru the hospital) is much less on the average than the alternative and avoidable cost of intra-mural hospitalization. The curative and rehabilitational extra-mural results are more rapidly achieved. They are more successful, and more stable, if only because the psychological subsidy is exhibited more intimately in home surroundings. Moreover, environmental factors in which disease breeders may flourish are seen and dealt with in situ.

It remains to make provisions for the sick man who is (a) homeless, and financially helpless, or (b) whose home cannot be improved by subsidy, and who does not require initially, or no longer requires, a hospital bed. In this case we are dealing with a complicating environmental problem of the first order. The method of choice here is not to permit homelessness or home-poverty as an excuse for hospitalization which is otherwise contraindicated, but to plan a substitute for his home (in the knowledge that such substitutes are possible, while substitutes for hospitals during illness requiring hospital care are not possible). In this case however the substitute home, whether individual or institutional, should bear the same extra-mural relationship to the hospital as the original home does under this plan. There are therefore three locations for the sick man, depending on social as well as medical factors: (a) the hospital proper; (b) his home; and (c) a substitute for his home, in all cases under hospital jurisdiction assisted by the practicing medical profession.

It remains to add that, having planned and reorganized for the patient suffering from prolonged illness we need not deny equally effective care to the patient suffering from acute illness who may likewise benefit on occasion from Home Care. The essentials of planning in any case are these: (a) that the traditional hospital rigidity of structure and function be reconsidered with these modern principles and opportunities in view; (b) that the principle of flexibility in all aspects of hospital activity be made a fundamental requirement of hospital planning and policy, available for application on short notice; (c) that the home be appraised anew with a view toward improving it and making it a valuable adjunct to the hospital during illness, increasing its bed capacity to this extent; (d) that the environment of the patient (in home and hospital) be studied inclusively for the purpose of neutralizing, or at least minimizing, disease-breeding situations of whatever nature; (e) that portable equipment be made available to both sides of the hospital wall; (f) that the practicing physician be assimilated into such a program, to his greater professional and economic advantage; (g) that the patient be studied from all angles continuously, without any other consideration than his needs and the needs of the doctor who serves him; and (h)

* Bluestone, E. M.: "Extra-Mural Hospital Beds", The Modern Hospital, **65**: 44–45, September, 1945. Bluestone, E. M.: "The Principles and Practice of Home Care" J.A.M.A. **155**: 1379–1382, Aug. 14, 1954.

that such a program of medical care be submitted to community authority as a matter of self-interest, as well as citizen protection.

The by-products of the reorganization of home and hospital to meet the needs of prolonged illness or, for that matter, of any phase of illness, are numerous, prolonging life and promoting comfort. This is the road to better and better medical coverage, and particularly so if it is supported by some method thru which the costs of medical care (in home as well as hospital) can be distributed over a large number of individuals thru a pre-paid insurance plan (of which Blue Cross for hospitalization is only one example). The costs for hospital construction, and subsequent maintenance costs to the community as a whole, are far greater under the prevailing policy of separation, independence, and fragmentation of medical care which tolerates the establishment of superior institutions for the acute strategically, and inferior institutions for the "chronic" at a distance, while the priceless asset of the home is disregarded. Everything that is happening in our own time to advance the cause of social, clinical, and laboratory medicine, has made the path of reorganization more rewarding, more humane, and less expensive. It remains only to adjust hospital progress to medical progress to the end that all members of society during illness will command exactly what they require when they require it.

The Edward Bell Krumbhaar Award in Medical History[1]

By STANLEY P. REIMANN, M.D.[2]

WE HAVE COME this evening to witness the giving of the first Edward Bell Krumbhaar Award in Medical History to two students whose theses have won them this honor.

Who is Dr. E. B. Krumbhaar, that his name should be attached to this award? There he is in the audience, and he is interested in the proceedings. You all know him, but just to refresh your memory of what sort of person he is and what he has done, I was asked to say a few words from the point of view of a brother pathologist. His accomplishments along historical lines will be touched upon by Dr. Radbill. We'll all be interested in hearing about these too, for we are all children of the past and the past has had quite a share in molding us. The story of a man with Dr. Krumbhaar's accomplishments up to date—and they certainly are not finished yet—cannot be told in a few words nor in a few remarks. Just a sketch or two will have to suffice.

Dr. Krumbhaar was born in 1882, but the years have dealt very kindly with him. When I did myself the honor of calling on him several weeks ago, I found his physiological age quite a bit younger than his chronological age. To bear out my remarks that he will accomplish more than he already has, I found him interested in all sorts of human activities, from the history of a man named Cruikshank (not the famous one, but his brother) to the transplantation of nuclei from one cell to another.

He, like many of us, in a wistful kind of tone said he wished that he could keep up with the new chemistry. I sympathize with him, as no doubt most of you do. All of us know full well the value of translation of the descriptive terms of our art in pathology to the more precise terms of chemistry and physics. And so Dr. Krumbhaar, knowing this, was a little wistful, but realized the importance of this to us pathologists, and floundered along a bit—yes, this is the word, "floundered"—for what with chromatograms, resin columns, electrophoresis, unsaturated electron bonds, etc., etc., what can the pathologists do? The language is difficult, even though some of the concepts are intelligible enough. These Dr. Krumbhaar is well aware of, and I mention it just to show you how his interest is unabated in finding out more about how nature works.

I'll tell you that he graduated from Harvard in 1904, from the University of Pennsylvania with an M.D. degree in 1908 and a Ph.D. in 1916. His interest in medicine, however, began earlier than that, for while still a boy Dr. Orville Horwitz took him to the Jefferson Hospital to see and learn about various operative procedures. His first publication, entitled "The Growth of our Knowledge of Adams-Stokes Disease", was written for the H. C. Wood Medical Society of the University of Pennsylvania. Dr. Longcope of Philadelphia, and later of Baltimore, was one of his teachers and he roamed into neuropathology with him—writing up a case of polio-encephalitis superior.

Harold Austin, whom we all knew and respected, was with him when he studied in Vienna. This, it will be remembered, about that time (1906) was a Mecca for many students, particularly those wanting to learn

[1] Section on Medical History, College of Physicians of Philadelphia, 12 February, 1957.

[2] Director of the Lankenau Hospital Research Institute, Scientific Director of The Institute for Cancer Research, Professor of Oncology, Hahnemann Medical College and University of Pennsylvania Graduate School of Medicine.

something of pathology. He then became Resident Pathologist, putting what he knew to work—and learning more, at the Pennsylvania Hospital in 1908 and 1909, and later was Resident Physician at the Pennsylvania Hospital. With his background of pathology he turned a bit toward internal medicine, working with Dr. Alfred Stengel, Professor of Medicine at the University of Pennsylvania. Later Dr. Krumbhaar shifted to pathology and directed the laboratories of the Philadelphia General Hospital from 1922 to 1927. In 1927 he became Professor of Pathology in the University of Pennsylvania, so went back to his first love, and there he remained for 20 years, until he became Emeritus Professor.

In the short time allowed me I can at least get a start on naming the societies of which he is a member. Perhaps I'd better just mention a few in which he played an active and constructive part as one of the officers. He was president of the Pathological Society of Philadelphia and of the Physiological Society, was president of our beloved College of Physicians of Philadelphia; president, too, of the American Association for Cancer Research; and not only was he president, but he was also a founder of the American Association for the History of Medicine. There are many other societies in which he played a part, but this is enough to remind us of his activities and of the creative work which he accomplished in medical society work.

He liked the spleen, the blood, and the bone marrow; the heart too, and many of his contributions are in that field. I have in my hand a sizable pack of cards listing the titles and where his communications appear. I might pick from these a few which I think he, himself, will consider of more importance than the others: here is one on reticulosis, published in 1922; here is one on the hematopoietic system in primary anemia; here are some on agranulocytic angina; here are several on cardiology—but I leave two for particular mention—for out of them has come a quite important application. He studied the blood and bone marrow in gas poisoning during the First World War, and the blood and bone marrow in yellow cross gas, i. e. mustard gas, poisoning. It is interesting to follow the story from then on up to today's use of mustards—in this case the nitrogen mustards of benefit in many cases of tumors of the reticulo-endothelial system, i. e. lymphomas, Hodgkin's Disease, and their ilk.

You, of course, know that he was editor of *The American Journal of Medical Sciences* for a good many years and kept this journal in high repute among clinicians and clinical investigators alike—with a dash now and again of results in so-called fundamental research. This, not-too-easy job (to be an editor) he did superbly.

In closing, when I was asked to make a few remarks (and I hope they were not too many for I could have made a lot more) I was honored indeed. In these remarks you will find some reasons why the name Edward Bell Krumbhaar is associated with the award which these two students, about to be presented to us, will receive: for his influence on pathology, for his contributions to scientific knowledge, for his being a real gentleman, for his contributions to medical history, and last but not least—for his being a good teacher, whose pupils carry on in the tradition of wanting to know and doing something about it.

Krumbhaar Prize Established

IN RECOGNITION of his outstanding contributions to medical history in this country and abroad, the Section on Medical History of the College of Physicians of Philadelphia has named its medical history essay contest prize in honor of Edward Bell Krumbhaar, past president of the College and emeritus professor of pathology at the University of Pennsylvania.

Winner of the first Krumbhaar Award for the best essay submitted by medical students from Philadelphia's five medical schools was Dr. Marshall Smith of New Brunswick, New Jersey. Dr. Smith, a 1956 graduate in medicine at the University of Pennsylvania now interning at Hartford Hospital in Connecticut, received the one hundred dollar cash prize and certificate for his essay on "Leonardo Da Vinci and Andreas Vesalius—A Comparison." Honorable mention was awarded to Dr. Stuart H. Shippey, Jr. of Philadelphia, who also received his M. D. degree last year at the University of Pennsylvania where he is now serving his internship. Dr. Shippey's essay concerned "Sketches of Past Professors of Medicine in the University of Pennsylvania." These papers will appear in future issues of *Transactions & Studies of the College of Physicians of Philadelphia.*

Left to right: Dr. Nicholas Padis, Chairman of the Section on Medical History, Dr. Stuart H. Shippey, Jr. (Honorable Mention); Dr. Krumbhaar; Dr. Marshall Smith (Prize essayist), Dr. Lewis C. Scheffey, President of the College of Physicians of Philadelphia.

Dr. Krumbhaar, who celebrates his 75th birthday this year, presented the awards at the section's meeting at the Hall of the College on February 12, 1957. Dr. Lewis C. Scheffey, President of the College, and Dr. Nicholas Padis, Chairman of the Section on Medical History, presided at this meeting. Dr. Stanley P. Reimann of Lankenau Hospital, and Dr. Samuel X Radbill, Past Chairman of the Section on Medical History, paid tribute to Dr. Krumbhaar's work in pathology and medical history on this signal occasion.

FRED B. ROGERS, *Clerk*
Section on Medical History

Edward Bell Krumbhaar: Medical Historian, Bibliophile and Humanist[1]

By SAMUEL X RADBILL, M.D.[2]

Edward Bell Krumbhaar ("Ned" to his intimate friends), is one of the last remaining members of a group of Philadelphia medical historians who placed this city in the forefront of national and world wide repute in the field of medical history during the first half of the twentieth centry. Francis R. Packard, David Riesman, William Pepper, Charles W. Burr, Burton Chance (the last of whom is happily still with us), all fellow members of our Section on Medical History of the College of Physicians of Philadelphia, by their writing, teaching and dynamic personalities, have also fired those of us who have been fortunate enough to have known them with the will to keep the torch of medical history glowing.

Dr. Krumbhaar graduated from the School of Medicine of the University of Pennsylvania in 1908. That very year he published his first medico-historical paper: "The Growth of Our Knowledge of Adams-Stokes Disease" (1). This was an outgrowth of his work on heart block as a second year student when he chose the history of this subject as his assignment for a talk before his undergraduate medical society. Since then his interest in the history of medicine has never flagged. While it is true that his primary achievements in the progress of medicine of the half century that has passed since that time have been in the field of pathology, his enthusiasm for and contributions to the history of medicine have been continuous and contagious. During his student years there was a small coterie of his teachers who maintained a lively interest in medical history. They formed a medical history club at the University of Pennsylvania that met regularly, and from this association these men were instrumental in forming, in 1905, The Section on Medical History of the College of Physicians of Philadelphia. This Section, except during the war years, has held regular meetings for over fifty years. Its objectives have been to bring distinguished medical historians from other cities to Philadelphia, to arouse interest in medical history, and to further the production of a great deal of important writing and discussion on the subject. From the time of his election as a Fellow of the College of Physicians of Philadelphia in 1914, Dr. Krumbhaar has been actively interested in this Section. He has served as clerk, chairman, and on the executive committee, has participated in its discussions, has frequently presented papers which soon appeared in print, and has attracted notable men from all parts of the world to speak here on the humanities and on cultural aspects of medicine. His influence has been a great inspiration to us all.

From the day in 1914 when he became a Fellow of this College of Physicians of Philadelphia, Dr. Krumbhaar has taken an active and leading position in all its affairs. He has served on many committees, on the Council of the College, and as its president. His love for books and the medical humanities has led him to foster especially the leading position in this country of the College in the study of medical history and the preservation of books, manuscripts, letters and other objects of historical value through the College Historical Collections and through our Section on Medical History. For more than forty years, as pointed out by Dr. W. B. McDaniel, 2d, scholarly Curator of the Library Historical Collections (2), the library's annual reports have been

[1] Presented before the Section on Medical History, College of Physicians of Philadelphia, 12 February 1957.

[2] Past Chairman, Section on Medical History, College of Physicians of Philadelphia.

noting acquisitions donated by Dr. Krumbhaar. In 1950 alone, he presented some 200 rare volumes, among which might be mentioned works by Botallo, Ficino, Galen, Fioravanti, Montanus, Peter Lowe, Thomas Bond, Claude Bernard and an 1802 early American edition of Jenner's "Inquiry."

In 1914 he read before the Section on Medical History of this College a "History of the Extirpation of the Spleen," a paper stemming from his important studies in the pathology of that organ (3). Subsequent papers read before the Section included "Some Medical Medals and Tokens" (4), "The Early Days of the Oldest Medical Monthly, *The American Journal of the Medical Sciences*" (5), and "The Stigmata of St. Francis of Assisi" (6).

When the International Association of Medical Museums published a Memorial Number (7) dedicated to Sir William Osler in order to show the relations of that great medical humanist to pathological studies and researches, Dr. Krumbhaar was called upon to serve on the editorial committee. He himself contributed a paper on "Osler's Connection with the College of Physicians of Philadelphia", which reveals Krumbhaar's characteristic zeal in tracing minute details that are so necessary in accurate historical recording. In this article he tells of Osler's curious interest in the College's "Siamese Twins" collection, and of Osler's admonition to "Try to make your Siamese Twin collection as complete as possible," saying "The opportunity for carrying out this idea still awaits an enthusiastic follower." As usual in such cases, the "enthusiastic follower" turned out to be a firm proponent of the do-it-yourself principle. Dr. Krumbhaar himself had in 1923 compiled and arranged a relic list and bibliography of the Siamese Twins at the College of Physicians of Philadelphia, pertaining to the famous Chang and Ching twin.

Upon the one hundreth anniversary of Osler's birth, Krumbhaar was again asked to pay tribute to "The Great Physician" when the *Archives of Internal Medicine* dedicated one of its issues as a salute to Osler's memory (8). Dr. Krumbhaar's contribution consisted of "Additional Notes on Osler in Philadelphia (9)."

In 1929 his paper on "Bibliographical Matters Pertaining to the Discovery of the Circulation of the Blood, Based on the Tercentennary Exhibit of Harviana by the College of Physicians of Philadelphia" (10), besides exhibiting Krumbhaar's vast stock of historical knowledge, served again to call attention to the College of Physicians of Philadelphia as a rich mine of medical treasures of the past awaiting future exploitation.

In 1930 he also compiled a photographic collection of seventy-five printers' marks, ancient and modern, which can be studied at the Library of the College of Physicians. His Collection of Correspondence deposited with the College of Physicians' Library is also a rich storehouse of historical treasure, including correspondence concerning Base Hospital No. 20 (1917) of World War I with which he was associated; extensive archival material concerning the Department of Pathology of the University of Pennsylvania, *The American Journal of the Medical Sciences*, of which he was editor for many years; of the Council and other matters related to the College of Physicians of Philadelphia, including the records of the ceremonies commemorating the 150th anniversary in 1937, six boxes of correspondence concerning *Clio Medica*, and lots more.

In 1932 an 'Exhibit of Books and Memorabilia Illustrative of the History of Physical Diagnosis Throughout the Ages' was arranged at the College of Physicians for the Sixth Annual Students' Night. Dr. Krumbhaar aided in the preparation of this exhibit and provided many objects from his own private collection (64).

He had a great admiration for Karl Sudhoff who did so much to advance the study of medcal history in Germany, and was instrumental in bringing him to this city to speak at one of the meetings of the Section on Medical History, and upon Sudhoff's death, wrote an

obituary for the *Transactions & Studies of the College of Physicians of Philadelphia* (11).

When asked to address the Piersol Anatomical Society, a student group at the School of Medicine of the University of Pennsylvania, Dr. Krumbhaar expatiated on the "Lure of Medical History" and the many advantages that can accrue to the practicing physician from a respectable acquaintance with the history of our profession (12).

In 1922 he attended the Third International Congress on the History of Medicine where he met many of the leading medical historians of Europe. The International Society of the History of Medicine had been founded in Paris the year before and Dr. Krumbhaar came home imbued with the idea of organizing a national section in this country. Largely through his efforts, the American Association of the History of Medicine was thus organized in 1924 (13). He was truly the father of this association and guided it like a child through its difficult years. He worked on many of its committees, was secretary-treasurer during the first six years, was twice elected president, reviving it after a period of quiescence following the second World War, and has long (14) been honored as Honorary President. For a quarter of a century, so long as his health would permit, he never missed one meeting (15). At the coming meeting of the Association to be held in Richmond, Va., next May, his seventy-fifth birthday will be celebrated this year with appropriate cermonies that will express the affection and esteem his many friends hold for him.

In 1934 he presented before the American Association of the History of Medicine a paper on "William Hunter of Newport" who was one of the first to lecture on Anatomy in the British Colonies (16). With customary thoroughness he had searched every available source of information about this elusive Hunter (17). Among other papers given at meetings of the American Association was one on "New Contemporary Documents Bearing on the Death of King Charles 2nd" (18), and another with "Notes and Impressions on the Tenth International Congress in Madrid in September 1935" (19). He has been an enthusiastic attendant at these biennial international meetings, has frequently represented the American Association of the History of Medicine as its official delegate to the International Society of the History of Medicine, and in 1925 was one of the Honorary Vice-Presidents. His paper for the Congress that year covered "Seventeenth Century Medical Literature as Exemplified in The Elzevier Presses" (20). At another meeting his paper dealt with the history of "Early Medical Journalism in North America" (21). Regarding the meeting in Athens, Greece, he sent a lively report in a letter to the editor of the *Journal of the American Medical Association* (22) hoping to bring attention to a wider audience throughout the country, to the work being carried on in the field of medical history.

In 1930 Dr. Krumbhaar inaugurated a series of "Primers on the History of Medicine" under the euphonious title of "Clio Medica" which was intended to present the history of medicine in handy booklet form, covering individual phases of the subject in concise, yet readable manner. Thus he hoped to entice as readers the medical undergraduate, the specialist, the busy general practitioner and the intelligent layman, and awaken in them an interest towards a more comprehensive study of the subject. The result was a collection of twenty-two volumes published during the next decade by some of the most brilliant medical historians of this generation. Dr. Krumbhaar's profound knowledge of the subject matter and history of pathology eminently qualified him to be the author of the nineteenth volume of the series devoted to the history of pathology (23); and in addition, he translated into English the volume on "French Medicine", originally by M. Laignel-Lavastine and M. Raymond Molinery (24), and the one on "Italian Medicine" by Arturo Castiglioni (25).

Dr. Krumbhaar has also brought before the English reading world other foreign language

works in the medical humanities. For Karl Sudhoff's volume of "Essays in the History of Medicine" brought out in 1926 by the Medical Life Press of Victor Robinson, he translated "Medicine and Art" (26), "Goethe and Johannes Müller" (27) and, in conjunction with Herman T. Radin, "Goethe and Maximiliane Von La Roche" (28). His translation of Arturo Castiglioni's "History of Medicine" from the Italian in 1941 was received with widespread approval for it filled a gap in the English literature that was sorely needed. A second, enlarged, edition was brought forth in 1947. When a volume of "Essays in the History of Medicine" was presented to Dr. Castiglioni on the occasion of his seventieth birthday, Dr. Krumbhaar joined with W. B. McDaniel, 2d, Librarian of the College of Physicians of Philadelphia, in contributing a paper on two early dissertations on diphtheria (29).

For Max Neuburger's "Essays in the History of Medicine", he translated the Viennese historian's "Ferdinand Von Leber's Services in the Abolition of Torture in Austria (30)"; to an Anniversary Volume in Honor of Joseph Hersey Pratt on his sixty-fifth birthday in 1937, he likewise contributed a paper; for a volume entitled: "Science, Medicine and History", published in 1953 to honor Charles Singer, he wrote an essay on "The State of Pathology in the British Colonies of North America" (67); and for Gould's "Pathology of the Heart" he wrote the first chapter on "The History of the Pathology of the Heart" (68).

In 1926, when Dr. Krumbhaar was president of the Philadelphia Pathological Society, the William Wood Gerhard gold medal award was established and Dr. Krumbhaar publicized the facts concerning this medal (31). A gold medal was presented to Dr. Krumbhaar, himself, in 1924 by Pi Gamma Nu, an honorary Greek letter society of social science. At the recent 100th Anniversary Meeting of the Philadelphia Pathological Society (69), he spoke to his fellow members about "The Worthy Past of Our Society."

In 1933, Medical Life devoted three issues to the story of "Old Blockley" on the occasion of the Bicentennary Celebration of the Building of the Philadelphia General Hospital. Dr. Krumbhaar's contribution was "The History of Pathology at the Philadelphia General Hospital." (65).

To *Medical Life*, that valiant effort of Victor Robinson, the "Don Quixote of Medical History," to vitalize medical history in this early journal on the subject in the English language, Dr. Krumbhaar sent for publication a report of the Fifth International Congress on the History of Medicine (66) and his paper on "The Early Days of the American Journal of the Medical Sciences" (5).

To the University of Pennsylvania Library *Chronicle* he was also a contributor, writing about "Shakespeare's Garden on the University Campus" (32), and an obituary of his fellow faculty member, Dr. Francis Randolph Packard (33). A memoir he wrote in the *Bulletin* on "The Letters of Benjamin Rush" could well have served as an introduction to this monumental collection edited by Butterfield (35). He reviewed many other publications in the domain of medical history as they appeared in the literature, such as the "History of Medicine" by Douglas Guthrie (36), "Geschichte der Alten Kölner Universität" by Adam Wrede (37), "Round About Harley Street" by C. P. Bryan (38), and "Lee on the Levee," (39) a historical novel by R. Cannon. But by far his most frequent essays in the field of medical history appeared in the *Annals of Medical History*, so ably edited by his friend and colleague, Francis R. Packard, and for which Dr. Krumbhaar was one of the associate editors in its later years.

Beginning with an exhaustive study of "The Early History of Anatomy in the United States" in 1922 (40), his contributions, notes, reports and book reviews in the *Annals of Medical History* appeared in a steady stream up to the close of that great journal in 1942. In 1923 he wrote on "The Post-Mortem Examination of Lord Byron's Body." (63). To the 1925

volume he sent a book review (41); "An Historical Retrospect of Experimental Cancer" (42) which was his presidential address to the Philadelphia Pathological Society; a report on the Fifth International Congress on the History of Medicine (43); a brief letter to the editor (44), and another book review (45). In the next volume appeared an editorial concerning the William Wood Gerhard Medal of the Philadelphia Pathological Society (46), and a paper on "Some Medical Medals and Tokens" which he had presented to the College of Physicians of Philadelphia with the hope of stimulating others to build up the College Collections in this field (4). The ninth volume opens with his paper on "The Stigmata of St. Francis of Assisi" (6) and also includes a report of the Sixth International Congress of the History of Medicine, before which group he had read a paper on "The Second William Oliver and the Bath Biscuit" (47). Two book reviews appear from his pen in the tenth volume (48).

Volume I of the New Series of the *Annals* contained his report of the Fifth Annual Meeting of the American Association of the History of Medicine (49); his paper on the Bath Olivers (50); a further review of the Dutch "Opuscula" that were a succession of books reproducing various Dutch medical classics (51); and the paper on "Bibliographical Matters Pertaining to the Discovery of the Circulation" (10) already mentioned. For the second volume of this series of the *Annals* he reported on the Sixth Annual meeting of the American Association of the History of Medicine (52); to the third, contributed a paper on "Erasmus Darwin and His Relation to the Doctrine of Evolution" (53); and in the fifth published an editorial on "Luesiana in the Library of the College of Physicians of Philadelphia" (54), and several book reviews (55). Succeeding volumes contained a report on the "Tenth Congress of the International Association of the History of Medicine" (56), a note on the "Centennial of the Army Medical Library" (57), a paper on "The Centennary of the Cell Doctrine" (which was the subject of an address given at Cornell University Medical College) (58), and another book review.

With the sixth number of Volume IV of the third series in November 1942, the *Annals of Medical History* came to a close with a valedictory by its editor, Dr. Francis R. Packard, and a final note of appreciation for Dr. Packard's noble efforts by Edward B. Krumbhaar. This note of appreciation (60) pays tender tribute to his friend and colleague who did so much to develop the study of medical history in this country. How nice it is to know that we now have a quiet niche set aside for us in the Library of the College of Physicians of Philadelphia which shall always be known as the Packard-Krumbhaar Alcove of Medical History.

Dr. Krumbhaar is an avid collector of books that have historical value. He has an uncanny knack for ferreting out these elusive milestones of medical progress. When he was pathologist at the Philadelphia General Hospital, he resurrected from a long-forgotten grave under the pathological laboratories of this ancient institution a treasure trove of old medical books, many of great rarity, which had been cast off by the unwitting modernists. I am sure he will be happy to know that our mutual friend Dr. Robert J. Hunter still carefully guards these treasures from predatory vandals.

Dr. Krumbhaar's acumen is highly regarded in the rare book market. When a highly desirable copy of Auvert's beautifully illustrated work on *Medical and Surgical Practice* escaped the grasp of one of Europe's famous collectors, Krumbhaar was suspect (61). Unfortunately, this time our man proved to be innocent. I think his love for books can best be expressed by a quotation he once chose from Cicero:

> "Literary pursuits employ youth, give pleasure to old age, make prosperity more prosperous; are a refuge and a solace in sorrow, amuse us when at home, do not hinder us in our duties abroad, make our nights less lonely and in our travels and

sojournings are our constant companions". (62).

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Oration on the Birthday of Medical Honors in America, by John Lawrence, 1768[1]

By HERBERT J. DIETRICH, JR., M.D.[2]

ONE of the pivotal documents—*sui generis*—in the annals of American medical history is John Lawrence's *Oration* dating from 1768. It was rediscovered last year by Dr. W. B. McDaniel, 2d, Curator of the Library Historical Collections of the College of Physicians, who immediately recognized the original Latin manuscript, in an excellent state of preservation, and exposed it to the fresh light of day from what might have been a century or two more of obscurity; for not only was the manuscript found among a vast accumulation of historical material (much of it unimportant) but the binding of it gives no hint of the importance of the text. Dr. McDaniel first described this rare volume and transcribed the Latin text in the issue of *Fugitive Leaves From the Library* for March, 1956.

A truly definitive document is not only a rarity but indeed the most reliable kind of historical evidence. It speaks for itself. It remains for the writer, in the case of the Lawrence *Oration*, to place it in perspective historically, to tell what is known about John Lawrence, and finally to attempt a translation of the Latin text into English.

The medical department of the then College of Philadelphia (later to become the University of Pennsylvania) matriculated its first students in 1765, the same year that saw the Stamp Act imposed upon the American colonies. The failure of colonial reform measures, in the political and economic spheres, was already evident. In the decade following, there occurred the turbulent events which were to culminate in the outbreak of the War of Independence. It was a period which threatened the survival of educational institutions in colonial America. Yet in such a climate American Academic Medicine was born and thrived; so that by June of 1768, the first class of eight men was ready to be graduated.

Carson[3] quotes from the minutes of the Board of Trustees of the College of Philadelphia an account of the ceremonies attending the first Commencement of the medical school, 21 June, 1768. Following a procession and various preliminaries, the first order of business was "A Latin Oration, delivered by Mr. John Lawrence, 'De Honoribus qui in omni aevo in veros Medicinae cultores collati fuerint [sic]' ".

One of Lawrence's classmates "in the first class of the first medical school in North America" was John Archer, a volume of whose medical notes in manuscript was recently presented to the University of Pennsylvania Library, and more recently described by Whitfield J. Bell, Jr.[4]

From Wickes' "History of Medicine in New Jersey",[5] we learn that Lawrence was born John, Jr., in Monmouth County, New Jersey, in the year 1747. He was one of seven children of John Lawrence, a surveyor. Concerning his early life we know nothing. He was graduated from Princeton College in 1764 where his record must have been a good one from the fact that so little of it remains. Amus-

[1] Read before the Section on Medical History of the College of Physicians of Philadelphia, 12 February, 1957.

[2] Fellow of the College of Physicians of Philadelphia.

[3] Carson, Joseph: A History of the Medical Department of the University of Pennsylvania . . . Philadelphia, 1869. pp. 69 ff.

[4] *University of Pennsylvania Library Chronicle* 22 (1): 1–8, Winter 1956.

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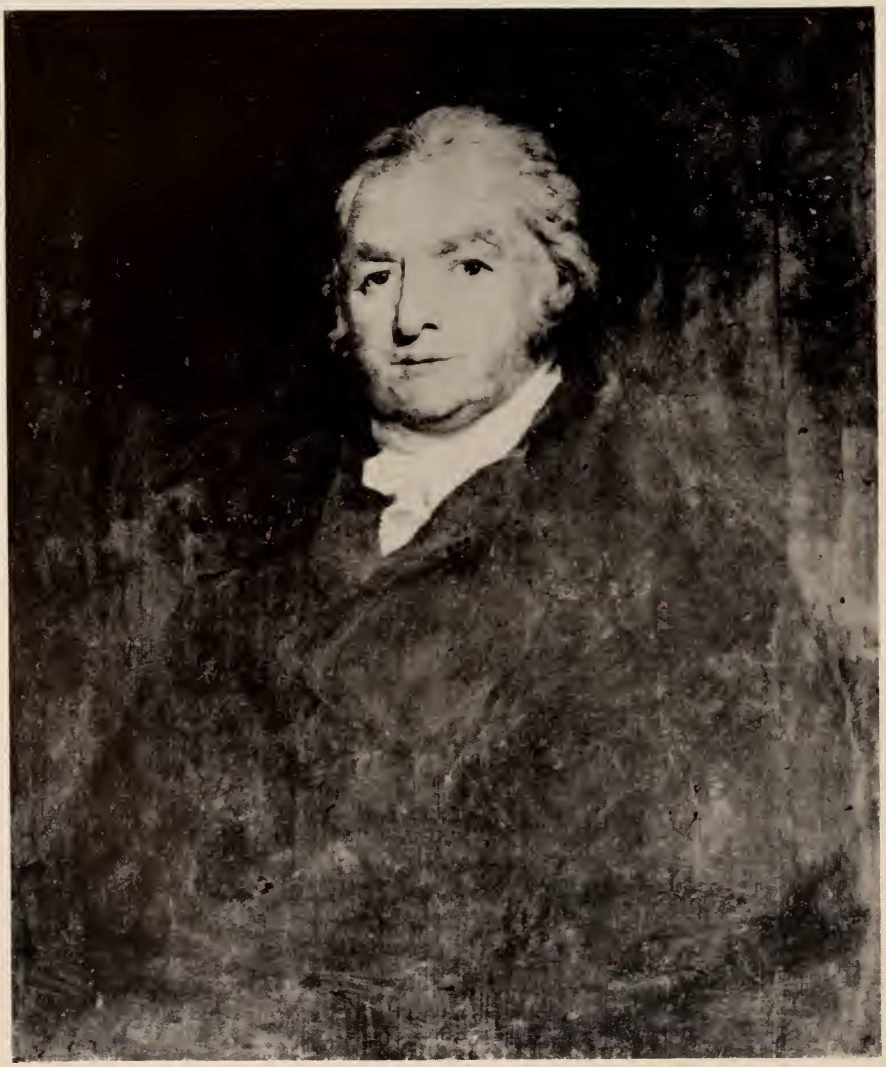
ingly, the present authorities of Princeton University tell us that in this early period it was the custom for the records of the students who got into scholastic or other difficulty to be kept at the President's house where, ironically, they continued to escape the flames which several times consumed the bulk of the records stored elsewhere!

Following his graduation from the College of Philadelphia, Lawrence returned to New Jersey where he practiced at Perth Amboy with notable success until the middle of the year 1776. About this time he found himself in difficulty with the authorities because, along with a good many professional men of his day, his political beliefs were those of Loyalist persuasion. Lawrence moved to New York City where he continued in practice until 1783. He then returned to Upper Freehold where he resided from that time onward. Apparently he had ample financial means so that he was not obliged to earn a livelihood through the continued practice of medicine. He was without family responsibilities, remaining a bachelor all his days, and thus found time to pursue a wide variety of interests. An excellent horseman, his favorite amusement was fox-hunting. He was said to be convivial and fond of games.



His death, at the age of 83 was said to have occurred while he was playing a game of chess during a visit to Trenton on April 29, 1830. Lawrence was buried in the Yellow Meeting House burial ground at Upper Freehold where one can see his epitaph today.

THE LAWRENCE ORATION

The complete manuscript of the Lawrence *Oration* is herewith reproduced for the first time, together with a reproduction of his portrait showing Lawrence as he appeared at age 65. The portrait reproduction was apparently acquired sometime after the text to which it was added; but we have no record of the dates of acquisition of either. The portrait is attributed to Thomas Sully, 1813, and it is hoped that the original will soon be located.

The Latin text, including a title page, appears on the rectos of 11 sm. 4° leaves. On the otherwise blank versos appear occasional reminders of the orator to himself, "Slow, loud, etc." The style of Latin is that of Quintilian. Admitted that some of it would probably have made Quintilian gasp and stare! If the punctuation seems appalling, one has to remember that rules for punctuation are of comparatively recent origin. Further, this is an oration and frequent pauses perhaps helped the audience to interpret it.

There is no doubt that Lawrence had a heightened sense of the importance of that historic occasion in colonial Philadelphia. He reviews the honors that have been bestowed upon physicians from the beginning of the human race, through various ages and among various peoples, right up to 1768 when Lawrence, with eight of his classmates, received the degree of Bachelor of Medicine. There could be no more fitting fanfare to announce the opening of the American tradition in Medicine than Lawrence's *Oration.* The forceful challenge to the future of the closing paragraph reminds *us* that history inspires if it does not always instruct.

Oratio, sive Sumo Academicus,
de honoribus quos gentes sapientissimæ,
& maximè celebres, in veros Medicinæ cul:
tores contulerunt —
a Johanne Lawrence habita —
primis publicis Academiæ commi:
tiis, ad gradus medicos conferendos, qui
pro gradu baccalaureatus in Medicina
prostitit —

Illustres Academiæ Curatores —
Qui his præses es dignissimus
Vir gravissime —
Viri reverendi facultatis academicæ ejusdem
Præses & Propræses amplissimi —
Professores facultatis academicæ clarissimi —
Cives dignissimi & Auditores, quocunque
Ordine, vel honore insignes,
vobis precor Salutem —

Exigit hujus Loci auctoritas, ut
de honoribus, qui in omni ævo, veris Medici:
:næ cultoribus collati fuerunt, verba faciam —
Artis Medicæ prima funda:
menta jecerunt, casus fortuitus, naturalis in:
stinctus, atque eventus haud prævisus —
Major deinde accessit arti perfectio, consti:
tutione Medicorum, tam ad morbos quosvis,
quam ad certos quosdam curandos, Annota:
:tione

:tione accurata morborum, observatione & descriptione, exacta, remedii & ejus usus — Cognitionem fabricæ Corpo:ris sani, causarumque abditarum & proxi:marum, tam sanitatis morbique, quam ipsius mortis, Extispicia Sacerdotum, Vul:nerum tractatio, incisio animalium in usus philosophicos, cadaverum balsamo condiendorum mos, et eorum inspectio attenta post Morbum tractatum, maxi:me promoverunt — Medicamentorum cognitio, præparatio, vis nota, eventusque observati, scientiæ herbarum, & chemiæ, & philosophiæ naturalis, operi fastigium fere imposuisse videbantur —

Non facile est, auditores spec:tatissimi, tempus definire, in quo Medicina habitum induerit, sive quod idem est, in quo selecti homines proprios se dederunt, gerendæ curæ valetudinis civium suo:rum — erat

~~erat~~ forte ante diluvium, erat forte a dilu:vio senex unus aut alter, suis vel Ali:orum casibus, aut propriâ quadem, ut homines solent, curiositate, in iis ver:satior, sibique placens; quæ humanam valetudinem lædunt, vel læsam, restitu:unt — talem fabulæ, antiquissi:mum historiæ genus, docent fuisse Phæ:bum, verum is Phæbus fuit Horus As:syriorum rex —

Probabile vero est Medicinam haud longé a Mesopotamia, primum ortum, duxisse, vel inde, quod ibi genus humanum natum sit, & primas inter Monarchias sedem ibi fixerit — In eadem felice et temperata regione, longævi Mortales plerasque Artes invenerunt — Medicina veró cum Astronomia & linguis, ~~inde~~ hinc in Phœniciam, ~~hinc~~ inde verò in Ægyptum migrasse potuit, et a Chaldæis præsertim exercita:ta fuisse — Ægytiorum plurimi medi:

Page 3: line 14—for *prima* read *primas*.

Medicinam fecerunt — Sacerdotes enim Ægyptii, Deorum, hominumque interpretes, dedecori non habuerunt, in apertis cadaverum visceribus inquirere — Antiquissimos ibi medicos fuisse, docet sacra Scriptura, quando mortui in Ægypto Jacobi corpus, a Medicis Josephi, balsamo conditum fuisse, narrat —

Apud Ægyptios, tanto fuit in honore ars nostra, ut ne Reges quidem ipsi, illam facere, infra dignitatem suam existimaverunt — Osiin & Isin, imprimis Reginam, medendi peritia excelluisse accepimus —

Videtur Amasis temporibus, quibus Græcis plurimum cum Ægypto commercium fuit, Medicina ad Græcos transiisse — hanc autem in Græcia derivatam floruisse, historia reliquit —

Hippocrates autem gente Asclepiadæa ortus, Artium & Scientiarum pulchra gnarus, suisque simul sapiens observatis, bona quæque adunando, corpus Medicæ græcæ conflavit, & primus veri nomen Medici meruit — fortunæ opibus valuit — in ipso medendi opere, felicitate mortales omnes superavit; in peste Attica, & Thessalica pene divinos honores mereri censebatur — Magno Nomini Hippocratis, adsurgimus omnes, qui non tantum sapientissimis præceptis hanc artem formavit, sed & ipse vita, & moribus, perfectissimi Medici Exemplar expressit — Tanto itaque viro maximos honores delatos, minime miramur, neque hos tantum a Coïs suis, qui Imagine ipsius, nummos signaverunt, sed etiam ab universa Græcia; quæ, ut narrat Plinius communi consilio, quod veniem ab Illyricis pestilentiam prædiperat, dis-

Page 4: line 12—for *existimaverunt* read *existimarent*.
line 15—for *Nidetur* read *Videtur*.

Page 5: line 9—for *maereri* read *mereri*.
line 16—for *miramar* read *miramur*.

discipulorque ad auxiliandum circa urbes demiserat, honores illi, quos Herculi decrevit — Civem porro adscipserunt Athenienses, auro coronarunt, & victum illi, & posteris, in Prytaneo dederunt, qui honor in Græcia maximus habebatur —

Athenienses cultissimi Scientiarum Æstimatores, hanc Artem plurimi semper fecerunt — et tam ab iis, quam ab aliis Græciæ Civitatibus, honores, & immunitates eximias, publicitus Medicis concedebantur —

Hanc, maximi, omni ævo apud Græcos, viri, Medicinam callere laudi sibi duxerunt —

Celeberrimus Aristoteles, medendi peritia, magni Alexandri benevolentiam sibi primum conciliavit, quem cum gravi Morbo oppressum liberasset, hanc ab eo facultatem, Rex invictissimus doceri voluit; neque illam exercere vile, aut a summa sua dignitate alienum, id ait Plutarchus judicavit —

A Græcis ad Romanos transimus; Romani, Artes omnes a Græcis acceperunt, & Julius Cæsar, in cujus manus summa rerum potestas devenerat, cum jam quotidie quotiis causa, et Græcia, Romam adirent Medici, omnes hanc Artem professos civitate donavit —

Antonio Musæ, postquam ejus Opera, et ancipiti morbo convaluerat Octavius Augustus, statuam, Ære collato, Populus Romanus posuit, Augustus quoque ei jus Annuli aurei, & immunitatem, non ipsi tantum, sed omnibus Medicinam professentibus, in posterum tempus concessit —

In summa, ita non semper tenui fortunâ homines Romæ erant medici, imo et etiam, imperatorum sæpe Amici essent & familiares —

ei

Si Medicinæ autem tempora, & varias quasi Ætates spectemus, ad Arabes jam, simul cum armis, literarum studia agitantes, nos deducit Orationis filum — Legimus quod apud eos, non tam ministri, quam consiliarii, imo Affines Regum, apud eos habebantur Medici — et terrarum Reditus, & Urbium præfecturæ, illis sæpe in Mercedem cedebant —

Postquam renascentibus literis, antiqui doctrinæ fontes recludi, & in Italia primum, inde et in cæteris Europæ regionibus, fervere studia Scientiarum cœperunt, apud alios, & alios populos, Medicina honores ~~xxx~~ varios sortita est, utque gloria aluntur Artes, ita hæc semper accepta beneficia, magnis in rempublicam Utilitatibus rependit — longum esset Scholæ ~~Salu~~ Salurnitanæ, Bononiensis, Patavinæ Monti-pessulani, Parisiensis, Leidensis, & aliarum Jura & immunitates explicare, verum illud memorare juvat, quod fama scholæ Edinensis medicæ, omnibus aliis, nunc temporis ~~præripit~~ palmam præripit; et nusquam honoratior, quam apud ~~Anglos~~ Britanos, extitit Medicina —

Dicant omnes Europæ gentes, dicant Britani tum in Europa, tum in Orbe Americano habitantes, quantum per Anglorum & Scotorum labores in Medicinæ studio, ipsi profecerint — Vivite æternum ~~Rutherford~~ illustria Nomina, Linacre, Caii, Harvei, Sydenhame, Mead, Pringle, Fothergill, Hunter — vivete Æternum Rutherford, Sinclair, Monro, Cullen, Whytte, Aliique præstantissimi, qui Medicorum Collegiorum, & Scholarum per sæcula maxime celebrium fundamenta jecistis & stabilistis, ~~xxxxx~~ nec non inventa

pulcherrima Mundum acquistis —

Lux nobis etiam affulget — gaudemus nostrates Medicos, nimirum veterum sapientium more, relictâ patria, terras longinquas adiisse, & semina omnis generis disciplinarum, quæ ad Medicinam excolendam pertinent, domum adtulisse —

Nobis Curatores illustrissimi, gratias habemus maximas, qui Scholæ nostræ medicæ ita favetis, & nostræ formam dare Reipublicæ medicæ vultis, quâ in unum corpus, quasi membra coërent Artis professores —

Ad vos autem mecum hac in Schola studiosi delectissimi, tandem se convertit Oratio, pergite per Studia vestra, famam hujus Academiæ in Altum Attollere — Ita nunquam deficiet Medicorum ingeniosorum & doctorum successio, qui humano generi saluti, qui sibi ipsis & patriæ, magnæ futuri sunt laudi & decori —

Doct
John Lawrence

Dr L

Oration, or Academic Discourse, Concerning the Honors Which the Wisest and Most Celebrated Peoples Have Conferred upon the True Cultivators of Medicine

Delivered by John Lawrence, a candidate for the degree of Bachelor of Medicine, at the first public convocation of the Academy for the conferring of degrees in Medicine.

HONORABLE Trustees of the Academy, whose president is a most learned and worthy man; revered members of the same faculty, most worthy president and vice-president; distinguished professors of the academic faculty; most worthy citizens here to-day, possessed of whatever rank or honor, my most reverent greetings to you.

The importance of this occasion demands that I speak about the honors which, through all times, have been bestowed upon the real champions of Medicine.

Chance occurrence, natural instinct and completely unforeseen events gave rise to the earliest beginnings of the Art of Medicine. Later on it acquired greater perfection under the aegis of medical men; and by their accurate "case histories" and observation of all sorts of diseases and—in the case of certain ones that could be cured—an exact description of a remedy and its use. Knowledge of the anatomy of the healthy body, of the obscure and common causes of health and disease, as well as death itself, was especially advanced by the following: the sacerdotal inspection of entrails, the management of wounds, the custom of embalming cadavers with balsam and their careful inspection after a disease had been discussed. A knowledge of medicinals, their preparation and known strength, the observed results; a knowledge of botany, of chemicals and natural philosophy: these seem for the most part to have crowned their work.

It is not easy, distinguished listeners, to pinpoint the time when medicine assumed the stature of an art, in other words to say just when particular men devoted themselves exclusively to the task of looking after the health of their fellow citizens. Perhaps before the flood—or maybe at the time of the flood—some old man or other, whether because of his own experiences or those of others, or because of a certain innate inquisitiveness, as men will, became more interested in and found satisfaction in the knowledge of what things afflict human health, or when afflicted what things restore it. This sort of fable, the most ancient form of history, teaches that it was Phoebus, the same Phoebus who was King Horus of the Assyrians.

It is likely, however, that medicine derived its origin not very far from Mesopotamia, or at least therefrom, because the human race was born there—and that there among the early kingdoms it established a place for itself. In this same fertile and temperate climate the ancients acquired a good many arts. Doubtless medicine, along with astronomy and the languages, was able to move from here into Phoenicia and thence actually to Egypt; and it was practiced especially by the Chaldeans. A great many of the Egyptians pursued the Art of Medicine. Indeed the high priests of Egypt, the mediators of the gods and men, did not consider it undignified to examine the exposed organs of cadavers. The Bible* tells us that there were most venerable physicians there, and that the body of Jacob, when he

* Genesis 50:2.

died in Egypt, was embalmed with balsam by Joseph's physicians.

Among the Egyptians our art was so esteemed that not even kings themselves considered it beneath their dignity to practice it. Osiris and Isis, especially the queen, we have believed, were pre-eminent in their knowledge of healing.

It appears that in the time of Amasis, when the Greeks carried on a great deal of trade with Egypt, Medicine crossed over to the Greeks—and history makes is abundantly clear that this art, brought from Egypt, flourished in Greece.

And now Hippocrates, offspring of the Aesculapian family, having a thorough knowledge of the arts and sciences plus a lot of common sense of his own, by combining everything good, brought together the substance of Greek Medicine, and he was the first actually to deserve the name of physician—and with the help of luck he succeeded—for in his flair for the art of healing he excelled all mankind. In the Attic plague and in the Thessalian one he was considered to merit almost superhuman honors. We all revere the great name of Hippocrates who not only gave character to this art [of ours] through his brilliant teachings, but the man himself, in his life and manners, was the ideal of the complete physician. And so we scarcely wonder that the greatest honors were conferred upon such a man; and these not merely by his contemporaries [in his native island] of Cos, who struck coins in his likeness, but also by the Greek world at large; a representative assembly of the Greek states voted him the same honors it had [voted] to Hercules, as Pliny tells us, after Hippocrates had predicted the spread of an epidemic from Illyria and rushed his students to the aid of nearby towns. In fact the Athenians enrolled him as a citizen, crowned him with gold and gave him and his followers a banquet in the city hall—which in Greece was considered the greatest honor.

The Athenians, devoted though they were to the sciences, esteemed our art above all; and not only by them but also by the other Greek states, honors and extraordinary privileges were granted to physicians at public expense.

The greatest men in every age of Greece regarded it an honor to be skilled in the Art of Medicine. When the renowned Aristotle by his medical skill had won the friendship of Alexander the Great, whom he had liberated from the throes of a severe illness, the royal conqueror wanted to be taught this skill by Aristotle; nor, as Plutarch tells us, did he think it was common-place or beneath his dignity to practice it.

From the Greeks we pass on to the Romans; the Romans inherited all their arts from the Greeks; and Julius Caesar, into whose hands had come the greatest political power, (since every day Greek physicians were arriving at Rome to find employment) conferred citizenship on all professing this art.

To Antonius Musa the Roman people erected a statue of bronze that had been collected, when as a result of his services Octavius Augustus had recuperated from an extremely dangerous illness; and Augustus also granted him the right of wearing a golden ring, a privilege not long his alone, but soon extended to all practitioners of medicine. While on the one hand physicians at Rome were never out of favor with fortune; on the other hand they would often be the friends and intimates of the emperors.

If now we consider the eras of medicine, its various epochs as it were, the thread of this discourse leads us to the Arabs who vigorously applied themselves to the pursuit of letters as well as to the arts of war. We read that with them physicians were considered not so much public servants as advisors, indeed often the in-laws of kings; and the superintendence of towns and property rents were often given to them in fee.

When in the renaissance of literature the ancient sources of learning were being revealed, first in Italy and then elsewhere in Europe, the pursuit of scientific inquiry was all the rage with some, while among others Medicine shared diverse honors; and just as

praise nourishes the arts, in the same way medicine, often the object of favors, repaid the state in kind by its great serviceableness. It would be tedious to relate the powers and privileges of the school of Salerno, of Bologna, Padua, Montpellier, of Paris, Leyden and the others, but it is a pleasure to speak of a special one, because the fame of the School of Medicine at Edinburgh steals away from all the rest the limelight of our time; and nowhere has medicine stood more respected than it is by the British.

Let all the nations of Europe tell and let the British, living first in the European and then in the American sphere, say how much they have advanced through the contributions of the English and Scotch in the study of medicine. Live on forever O' famous names of Linacre, Caius, Harvey, of Sydenham and Mead and Pringle, of Fothergill and Hunter! Through all times live on O' Rutherford, Sinclair, Monro, Cullen, Whytt and other outstanding men, you who have established and supported the medical colleges and especially distinguished schools through the ages, you who have indeed made mankind aware of your priceless discoveries.

And now the bright dawn of our own day appears. We rejoice that our own native physicians, truly in the manner of ancient scholars, have left home and travelled to far off countries and brought home the elements of every kind of instruction which has to do with the advancement of medicine.

To you, distinguished trustees, we are especially grateful, you who so befriend our Academy of Medicine and desire to give a character to our medical affairs with which the leaders of our art may identify themselves, the members as it were, in one body.

And now finally this discourse concerns itself with you, my fellow students in this school; strive through your efforts to raise to the highest the reputation of this Academy. Accordingly, there shall never be lacking a succession of intelligent and skilled physicians, who in their concern for the health of mankind will have been a great credit to themselves and their country.

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The Use of the Radioisotopes as an Experimental Tool[1]

By EUGENE M. K. GEILING[2], PH.D., M.D.

INTRODUCTION

The Atomic Age—Its Inception, Significance and Challenge

THE Atomic Age began on December 2nd, 1942 when a crucial experiment, planned for many months by a corps of outstanding scientists, proved conclusively that the energy of the atom could be released and *controlled*. Expressed more simply: this momentous experiment demonstrated the feasibility of splitting the atom and controlling the release of astounding amounts of energy. Man was thus suddenly faced with the awesome responsibility of having at his disposal a potential source of energy many, many million times greater than ever before. Man's employment of the products of this discovery has already altered the course of history, and brought about revolutionary changes in our living and thinking (1, 2). The birth of the Atomic Age is a most important milestone in the history of the world.

In his recent book, *Atomic Quest* (3) Arthur H. Compton, a Nobel Prize winner and one of the leading scientists responsible for the development of the atomic bomb, gives a graphic account of the many researches and conferences which culminated in the successful experiment referred to above.

Everyone regrets that the first large-scale use of the products of atomic fission was for destructive purposes. The decision to do this was made by high ranking military officials in the expectation of bringing the war to a speedy end, and thus saving many human lives.

We must now meet the grave challenge of utilizing the products of atomic fission for constructive purposes. Fortunately, this challenge is being met, if one may judge by the vast number of research projects in practically every branch of the physical and biological sciences, human and veterinary medicine, agriculture, and in many branches of industry (4).

The scope of this vast undertaking can be gleaned from a perusal of the many Reports of the Atomic Energy Commission in Washington, D. C. One such report is worthy of special mention: *Isotopes—An Eight-Year Summary of U. S. Distribution and Utilization*, published by the U. S. Atomic Energy Commission, March, 1955 (4). This and subsequent ones to be issued periodically are intended to provide a source for quick reference to the many uses of isotopes. An extensive bibliography accompanies these volumes.

The nuclear reactor, or pile, in which

[1] Nathan Lewis Hatfield Lecture XLI, College of Physicians of Philadelphia, 6 February 1957.

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Uranium 235 is fissioned through a chain reaction process, is a source of radioisotopes in quantities much greater than ever available previously and at greatly reduced cost. Radioisotopes of all the stable elements can now be produced. So diversified and extensive have been the methods of artificially transforming atoms that it is now possible to make many more radioactive forms of atoms than the number of stable ones existing in nature. Of the 81 known elements there are only 270-odd stable isotopes whereas more than 900 radioactive forms of 100 elements have already been identified, most of which are made artificially. (4)

There are a number of nuclear reactors now in operation and more are being constructed. Admiral Lewis L. Strauss, Chairman of the Atomic Energy Commission, in a recent interview stated that at present the United States leads in the development of electric power from nuclear fission. He also stated that in a very short while the first complete atomic power plant designed to serve civilian needs will be producing 60,000 to 100,000 electrical kilowatts. This plant is being erected in the vicinity of Pittsburgh, Pa. (5).

At present a site is being prepared for the erection of a large nuclear power plant to be known as the Dresden Nuclear Power Station located about 50 miles southwest of Chicago, Ill. It is being financed entirely by private funds from the Commonwealth Edison Company and from the Nuclear Power Group, Inc. Construction is scheduled to begin early next spring (6).

USES AND CHARACTERISTICS OF RADIOISOTOPES IN BIOLOGY AND MEDICINE

Radioisotopes are employed mainly as (a) sources of ionizing radiation and (b) as research tools, especially as tracers.

(A) As *sources of radiation*, they are used in a manner similar to *x-rays and radium*. An example of such an isotope used as a source of radiation is radioactive cobalt (Co^{60}), a gamma emitter. It is known as "the poor man's radium" in therapy (7). One irradiated cobalt rod having 1800 curies of radioactivity costs $21,600, and is equivalent in radioactivity to four pounds of radium which costs about $36,000,000. This new source of energy enables moderate-sized hospitals to acquire facilities for treatment, which in the pre-atomic era were available only in large and well-endowed hospitals.

From a practical standpoint, Cobalt-60 facilitates the administration of radiation because of (a) ease of handling, and (b) destruction of healthy tissue and skin and muscle is reduced since the beam of high energy is easily concentrated on the tissue to be treated.

The cobalt source emits radiation equivalent to that of a 3,000,000 volt x-ray machine. The device which contains the cobalt is simple, while a 3,000,000 volt machine is a very complicated apparatus requiring constant service and maintenance (see illustrations (1)).

(B) As *tracers* radioisotopes are extensively used in many ways. The usefulness of radioisotopes depends on the fact that they emit various types of radiation which can be detected with such instruments as the Geiger tube, scintillation counter and ionization chamber. Moreover, radioisotopes enable one to trace materials in very minute amounts, much less than are detectable by physical, chemical or biological methods. They have unique characteristics and it seems as if Nature made them according to specifications as tracers.

One further advantage is that the radioisotopes are not foreign or chemically different from similar unlabeled atoms in the particular compound. For example, thiopental labeled with radioactive sulfur (S^{35}) is similar in all respects to unlabeled thiopental; the only essential difference being that the S^{35} in the labeled drug emits beta radiation which signals the presence of the unchanged drug or its metabolites. The radioactive isotopes have been referred to as natural tracers, to distinguish them from dyes or added chemicals which are used to follow a substance or to reveal its presence.

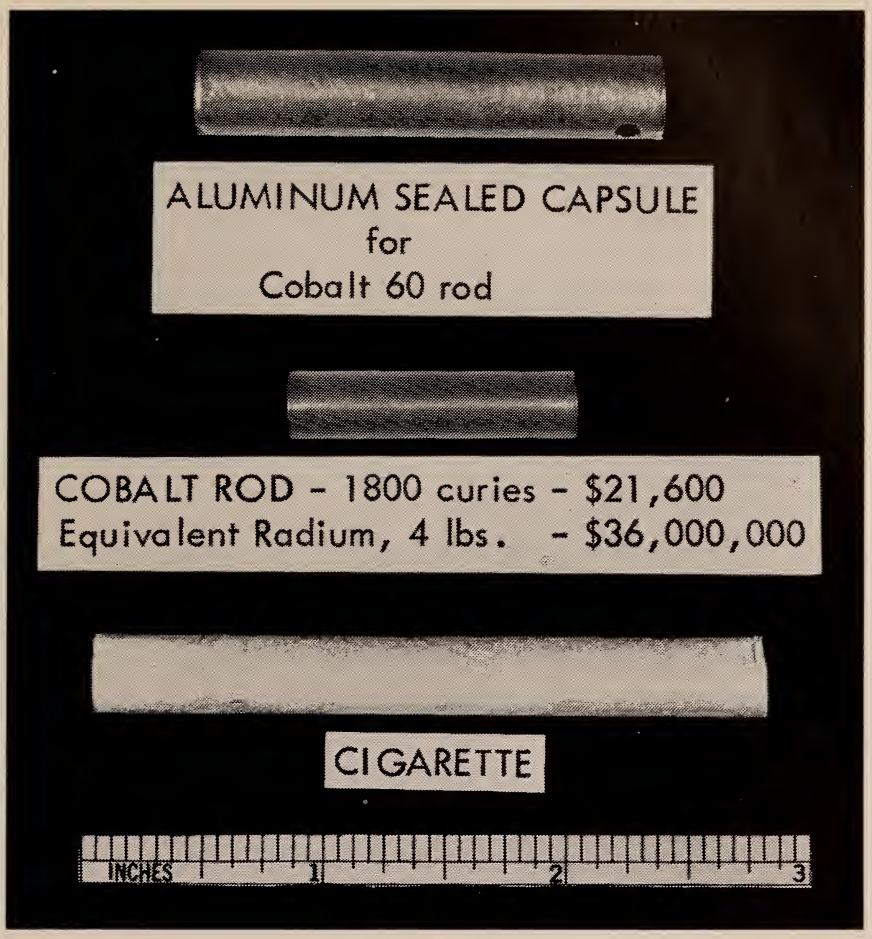

FIG. 1. Courtesy of Dr. L. Skaggs, Argonne Cancer Research Hospital

Sodium Radio-iodide Nai^{131} *(U.S.P. XV) and Radio-iodinated Serum Albumin (Human)*

At present, radio-iodine (I^{131}) is the most commonly used isotope in medicine. It has a short half-life (8 days), is easily administered, and does not require for assay equipment beyond that usually available in a well-equipped isotope laboratory.

Radio-iodine emits both gamma and beta radiation. The beta emission has weak penetrating power and is responsible for the inhibitory effects of the isotope on the tissues. The gamma, or penetrating rays permit a quantitative measurement of the isotope within the body, at the site of deposition, by applying either a Geiger or scintillating counter to the overlying skin surface. Needless to say, this valuable drug if improperly used, may be hazardous to the patient.

Sodium radio-iodine is used in (a) diagnosis of suspected thyroid disease, (b) treatment of selected cases of thyrotoxicosis in conjunction with other agents and methods, (c) in a small number of patients with carcinoma of the thyroid in which I^{131} served both for detecting and treatment of metastatic lesions when they are able to retain and metabolise the labeled iodine; its use is very limited for this purpose, (d) to induce hypothyroidism in euthyroid patients with angina pectoris to aid in the management of this condition.

The accumulation of radio-iodine in the thyroid gland probably reflects, to a large extent, the formation of diiodotyrosine and

thyroxine and the storage of these compounds in the thyroid follicle. At first, iodine may be present in the inorganic form (NaI), but in a short time it becomes protein-bound, apparently linked with the tyrosine radical, in the gland. Patients who have little or no functioning thyroid tissue, particularly with the clinical syndrome of myxedema, usually excrete considerably more of the diagnostic dose in the urine during the first 24 to 72 hours than do normal subjects. The uptake of radio-iodine may be depressed by prior intake of stable iodine in any form or by the use of thyroid substance or of antithyroid drugs.

Other antithyroid drugs, particularly those of the thiourea series and methimazole, also influence the uptake of radio-iodine by thyroid tissue. The quantitative uptake of radio-iodine by malignant tumors of the thyroid varies in accordance with many factors including their histological differentiation.

The uptake of radio-iodine by the thyroid may be influenced by large variations in dietary iodine content, and also by iodine-containing diagnostic drugs, such as iodopyracet (diodrast) (8).

Radio-iodine has been used in the palliative treatment of selected cases of inoperable carcinoma of the pancreas. The technique involves threading the tumor mass with polyethylene tubing into which is injected a solution of radio-iodine. A considerable relief has been obtained in a significant number of patients (8).

Radio-iodinated Serum Albumin (Human)

Radio-iodinated (I^{131}) serum albumin (human) is a stable preparation made by mild iodination of normal human serum albumin. It does not differ appreciably in properties from the original protein, and when injected intravenously there is no transfer of radioactivity to other blood proteins. It thus behaves like the normal plasma constituent. Complete mixing with the circulating blood occurs within ten minutes after intravenous injection. The urine is the chief route of elimination of I^{131}.

Radio-iodinated (I^{131}) serum albumin is useful as a diagnostic aid for tracer studies in the determination of blood or plasma volume, circulation times or cardiac output, and as an adjunct to other diagnostic procedures in the detection and localization of brain tumors. Its employment for determining circulatory volume and time, and for measuring cardiac output is based on the principle of dilution of tagged albumin in normal albumin pools of the body (9).

Radioactive Phosphorus. Sodium Radiophosphate (P^{32}) solution (U.S.P. XV—first supplement) is the next most commonly used isotope. It has a half-life of 14 days, and is a beta emitter. It is a constituent of all living cells and hence is widely distributed throughout the body. It concentrates in bone, blood-forming organs, and rapidly proliferating tissues. Radio-phosphorus is being successfully used in the treatment of selected patients with polycythemia. The radio-isotope exerts a palliative effect by suppressing red-cell formation to nearly normal levels which can be maintained either after a single large dose or repeated small doses. X-rays and other forms of treatment are also successful, but the advantage of using the isotope is that it can be administered on an out-patient basis in a physician's office. Radiation sickness and other side-effects usually do not occur. Leukemia has not responded too favorably to therapy with P^{32}. The acute form of the disease does not seem to be affected; but about 50% of patients with chronic leukemia are satisfactorily controlled with P^{32} (10).

Radio-phosphorus is also used for localization of brain tumors and in diagnosis of ocular lesions (10).

Radioactive Sodium (Na^{24})

Radiosodium has a half-life of 14.8 hours and is both a beta and gamma emitter. In 1942, Dr. John P. Hubbard and his associates used this isotope to measure the blood flow in children at the Children's Hospital in Boston, Mass. They measured the velocity of blood flow in infants and young children by determining the time elapsed for radioactive saline

injected into one arm to appear in the opposite hand (11).

At present there are available a number of additional methods which need not be mentioned here. Suffice it to say that recently, when radioactive iodinated human serum albumin, mentioned previously, became available another drug for measuring the velocity of the blood flow was added to our diagnostic armamentarium.

PART II—THE ADVANTAGES OF RADIOACTIVE ISOTOPES IN PHARMACOLOGICAL RESEARCH

Chemical agents have been used as tracers in pharmacological research for many years. These were usually added chemicals with specific properties, or dye-stuffs. For example, phenolphthalein was added to certain cheap wines to distinguish them from the better quality ones. Many such examples can be cited.

The radioisotopes are particularly suitable for pharmacological research because they are "natural tracers." This implies that the radioactive drug is composed of the same atoms as the nonradioactive one. Within certain limits they are alike chemically and pharmacologically, except that some atoms of the labeled drug are radioactive and emit radiation which can be detected by use of extremely sensitive electronic instruments, such as the well-known Geiger Counter, the scintillation counter, or the ionization chamber. By means of this technique one is able to detect the presence of the minutest amount of a drug and its split products in all the organs and tissues of the body. By the simple additional procedure, addition of pure nonradioactive drug, one can separate the unchanged labeled drug from its metabolites or degradation products which can be identified by other procedures such as solvent extraction, paper chromatography, ion exchange or by the more refined counter current distribution. These newer methods have been employed very satisfactorily in the identification and characterization of many new biological materials which are often present in very minute amounts in the crude or starting material. A word of caution should be added here: radioisotopes should only be employed where the conventional methods of extraction and identification of drugs or their metabolites are not sufficiently refined. It is unfortunately true that isotopes have been and are being misused. Anyone using this new technique must be warned that it is not necessarily the easiest and most direct approach to the problem. Special precautions must be observed to obviate contamination of the laboratory and equipment. Furthermore, there are health hazards that must be guarded against.

A number of our most useful drugs have (1) complex chemical structures, (2) cannot as yet be readily prepared in the chemical laboratory, (3) are administered to patients in such small doses that, when distributed in the tissues and body fluids, the conventional biological and chemical methods are inadequate, (4) some of the available methods may be able to detect the unchanged drugs, but not the metabolites; (5) another important advantage of using labeled drugs is that they can be studied at a therapeutic or sub-toxic level. In the past, some drug distribution studies were subject to the just criticism that the doses used were much beyond the therapeutic level, and at times even in the toxic range. Experiments had to be done with such large doses, because the then available chemical and biological level lacked the sensitivity needed to employ small doses.

Research work with radioisotopically-labeled drugs is best done by a team of workers. In our particular project, we enlisted the cooperation of botanists, zoologists, organic chemists, and individuals trained in radioisotope techniques. Studies on patients were carried out in the Billings Hospital.

Methods of Preparing Radioactive Drugs

There are three general methods of introducing radioisotopes into drugs.

1. *Biosynthesis.*
2. *Classic organic synthesis* in the laboratory. The labeled element is introduced into the desired position in the molecule.
3. *Converting the pure drug into a tritiated*

form by exposing it to tritium gas (H^3) in a sealed tube.

Practically all of the labeling of the drugs used in our projects was done with Carbon-14 which has the following advantages:

1. Carbon is present in all organic compounds.
2. In the form of $C^{14}O_2$ it can easily be incorporated into growing plants.
3. It has a long half-life (over 5000 years) which makes long term experiments possible.
4. C^{14} emits only weak beta radiation which minimizes the health hazards, obviates shielding and can be readily measured.

Owing to the long half-life of C^{14} special care has to be exercised to avoid contamination of the laboratory apparatus and glassware. Contamination can be avoided by observing prescribed procedures in the cleaning of glassware, and proper disposal of waste residues. Frequent monitoring of the laboratory, and checks on the background are most helpful.

Quite recently, Drs. Okita and Achor have succeeded in obtaining small quantities of digitoxin and morphine labeled with tritium (H^3). Since the specific activity of tritium-labeled drugs is much higher than those labeled with C^{14}, special precautions in handling the material must be observed. A well ventilated chemical isotope hood should be available. Special techniques for cleaning glassware must be rigorously observed. The personnel must be examined periodically for the presence of tritium in the urine. The assay of the tritium presents a special problem which has been solved by the use of liquid scintillation counters.

The overall purpose of our project was to obtain medicinally important drugs labeled with Carbon-14, and to study their fate and mode of action in the body (12). The two methods used for obtaining the labeled drugs were biosynthesis and organic synthesis.

Preparation of Radioactive Drugs from Plants by Biosynthesis

Biosynthesis is the term used to describe the elaboration of a specific substance by a living organism—in our case medicinal plants. Since many important drugs have complex chemical structures and cannot be synthesized in the laboratory, biosynthesis is a logical method of obtaining these drugs with labeled atoms. One such technique employed by us is plant biosynthesis which involves the growth of certain drug plants in the presence of radioactive carbon dioxide in gas-tight, temperature controlled chambers. See illustrations (2).

We determined that after our plants were grown in these chambers in the presence of radioactive carbon dioxide ($C^{14}O_2$) for periods varying from six to eight weeks, all the organic components of plant were radioactive. The plants were then harvested, dried, and finely pulverized. This finely grown material was the starting point for the extraction of the labeled drug. Because of the small quantities of starting material, the known chemical methods of drug extraction had to be refined. This in itself was sometimes a very challenging research problem. An essential requirement in all tracer studies is that the labeled drug be pure and free of all contaminants. This was costly since our supply of the labeled drugs was limited and often we could not reclaim the amounts of the drug needed for characterization.

Since some plants produce drugs best when grown at a relatively high temperature (75–85° F.—Belladonna) and others are more efficient at lower temperatures (45–55°F.—Podophyllum), and since some bear fruit on a short daylength (ragweed) while others prefer a long day (Opium Poppy), the establishment of these optimal growing conditions of medicinal plants as related to drug content is one of the principal interests of our group. Our plant physiologist, E. Mika, has shown that a relationship exists between the night temperature and the morphine content of the opium poppy (13). By using his technique we have prepared 35 mgm. of C-14 morphine with a specific activity of 0.3 uc. per milligram.

In addition, techniques have been developed for following the uptake of normal and radioactive carbon dioxide by the plants in the glass chambers. The rate and the total quantity of

gas absorbed by these plants is measured over a 24-hour period. Thus, the total amount of normal and radioactive carbon taken up by plants over the total growth period in the chambers can be easily determined.

On the basis of our studies we believe that the advantages of biosynthesis by a medicinal plant are:

a) The plant doesn't discriminate between C-12 and C-14, thus the compounds made while the plant is growing in the presence of $C^{14}O_2$ are labeled.

b) Usually the carbon atoms in biosynthetically-labeled compounds are randomly labeled and we can obtain relatively high specific activities.

c) After the radioactive plants have been extracted for their desired active principle, the plant residues also yield radioactive sugars, amino acids and fats which can be reclaimed and used in other pharmacological studies.

d) When organic synthetic methods are not available, biosynthesis becomes the only method of preparation.

To date we have prepared by biosynthesis (12):

Radioactive
Digitoxin.....from *Digitalis Purpurea*
Radioactive
Morphine.....from *Poppy*
Radioactive
Colchicine.....from *Colchicum Autumnale*
Radioactive
Atropine.....from *Belladonna*
Radioactive
Nicotine.....from *Tobacco*
Radioactive
Podophyllotoxin.from *Podophyllum Peltatum*

Time permits us to discuss briefly only two of the drugs named above.

Studies with Radioactive Digitoxin

Perhaps the most important gap in our knowledge of the role of digitalis is its fate in the human body. This deficiency cannot be ascribed to the want of carefully planned researches by many competent investigators but rather to the fact that neither the biological nor the chemical methods of detection were sufficiently delicate to enable one to determine with accuracy the minute amounts of either the unchanged digitoxin or its metabolites within the body tissues. By using labeled digitoxin these difficulties are overcome.

Dr. George Okita and coworkers extracted radioactive digitoxin from the dried, labeled

PLANT CHAMBER FOR GROWING RADIOACTIVE PLANTS

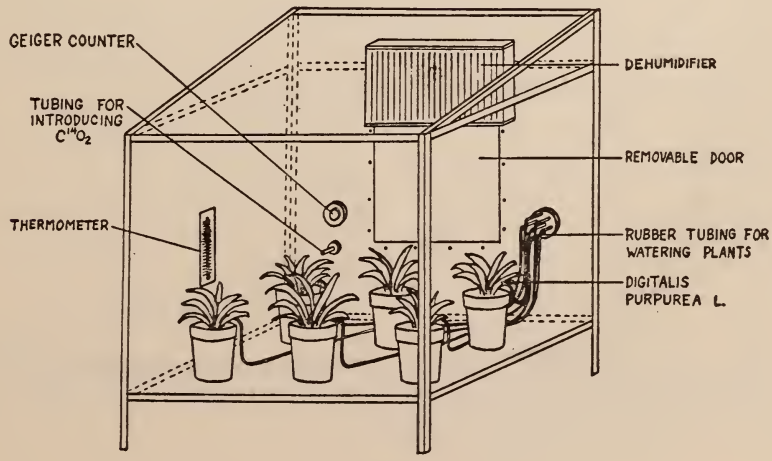

FIG. 2

digitalis leaves. The drug was then submitted to purification and characterized by the usual chemical methods: melting point, color reaction test, chromatography, etc. The first preparation (specific activity, 600,000 c/p/m/mg) was used on animals to compare the biological activity of the labeled drug with a pure unlabeled sample of digitoxin (14). The next step was to use this material in excretion studies in selected patients with congestive heart failure in the University of Chicago Clinics. The patients were given a therapeutic dose ranging from .5 to 1.2 mgms. The urine was collected over a period of days and daily estimations of the total radioactivity and the unchanged drug were carried out. The difference between the total and the unchanged drug represented the metabolites. This is the first experiment of its kind done with a therapeutic dose of the drug in which the quantitative estimations were made of both the unchanged drug and its metabolites (15), Fig. 3.

Similar studies were carried on with cardiac patients to determine the rate of the disappearance of the drug from the blood. It was found that the drug did not disappear as rapidly as was thought. After four days, there was still evidence of the unchanged drug in the blood. This may have been due to the release of the digitoxin bound to body proteins. This work is still being continued (16), Fig. 4.

Tissue distribution studies were carried out on three patients who were given the drug shortly before they expired. Tissue analysis for the unchanged drug and its metabolic products indicated that contrary to the previously accepted opinion, digitoxin does not have a high selective affinity for the cardiac muscle. Other organs such as the liver, the intestine, gall-

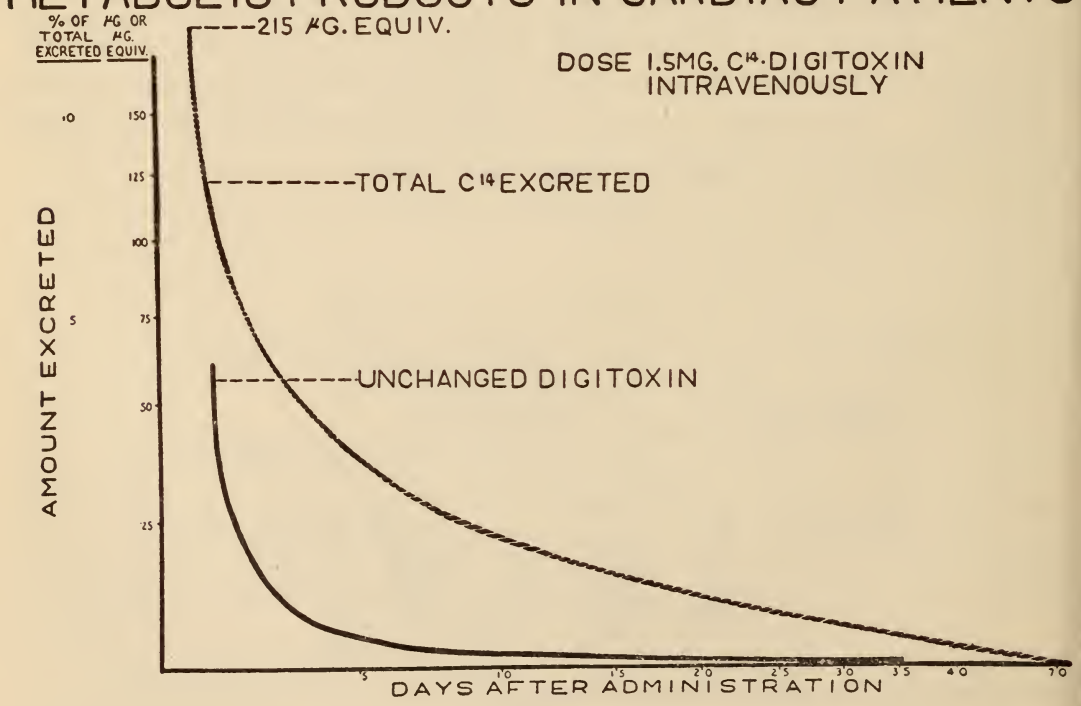

Fig. 3

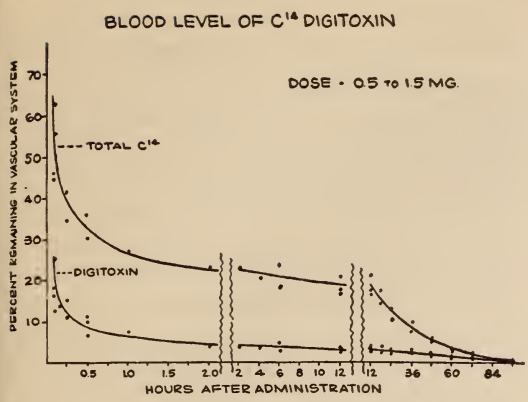

FIG. 4

bladder and kidney had higher concentrations of unchanged digitoxin than the cardiac tissue. Our studies indicate that the major organ involved in the metabolism was the liver. Our findings also indicate that enterohepatic cycling of digitoxin takes place. The major route of elimination of the labeled drug was found to be by way of the urine (17).

Placental transfer studies were first conducted in experimental animals and then in selected pregnant women in whom termination of early pregnancy was obligatory. From such studies, it was found that less than 1% of the administered digitoxin could be detected in the fetal tissues, indicating that therapeutic doses of the drug administered to pregnant women are not detrimental to the unborn child (18).

Tritiated Digitoxin

With the cooperation of Drs. K. Wilzbach and Weldon Brown from our Department of Chemistry, we have been able to obtain tritium-labeled digitoxin with a specific activity of 92 microcuries per milligram. The labeled compound thus obtained has been shown by appropriate tests to be radiochemically pure, and further, to possess biological stability. With high specific activity digitoxin, many experiments can be carried out which were previously limited by (a) the small doses of digitoxin employed and (b) the lower specific activity (0.7 uc/mg) of C14-labeled digitoxin (unpublished).

Digoxin

Studies recently carried out in this laboratory by Dr. Okita and Dr. Sidney Wright of the University of Sidney, Australia, have resulted in the identification of *digoxin* as a digitoxin metabolite. Although past evidence indicated the existence of this compound as a digitoxin end-product, the use of C14-labeled digitoxin enabled the execution of definitive experiments to prove its existence (unpublished).

Studies with C-14-labeled Morphine

The use of C-14-biosynthetically labeled morphine has provided us with valuable information regarding the mechanism of action of morphine and its antagonists. Studies by Dr. Leonard Achor and associates have shown that in the presence of either N-allyl normorphine or 5-aminoacridine, marked alteration of morphine distribution takes place in the experimental animal (mice). The systems most profoundly affected are liver, blood, kidney, and gastrointestinal tract (19). In addition to these changes, reversal of morphine antidiuresis also occurs (20), and correlates in time with the early release of morphine-C-14 via the urine in antagonist-treated animals (21).

Additional studies on the mechanism of morphine antagonism have utilized C-14-labeled glucose. In the presence of morphine, the ability of rat brain and liver to accumulate C-14 from administered glucose is markedly impaired; the administration of N-allyl normorphine, however, causes an almost complete reversal of the findings observed in the presence of morphine (22). We are at present concerned with the nature of the compounds in brain and liver which contain the C-14 from labeled glucose. Evidence thus far obtained implicates the Citric Acid Cycle. On this basis, the individual acids will be determined both quantitatively and for C-14 content, as soon as available methods are refined to enable accurate determination.

Many critical experiments have been hampered by the lack of adequate amounts of labeled morphine; we have attempted to cor-

rect this situation by incorporating tritium (H^3) into the morphine molecule. The labeling procedure is rapid, inexpensive, and provides a product with specific activity several hundred times greater than that of our C-14-labeled morphine. At present we are in the process of determining the stability of H^3-morphine in biological systems; if the results are satisfactory, we shall have available an adequate supply of labeled morphine (unpublished data).

Organic Radiochemical Synthesis

During the past two years in our department, a modern synthetic laboratory has been equipped with all the required safeguards needed for radiochemistry in accordance with the specifications of the Atomic Energy Commission. These include stainless steel benches, sinks and hoods with independently controlled filtered ventilation, vacuum lines in ventilated hoods. Dry boxes and high pressure hydrogenation equipment have also been installed. This laboratory is under the direction of Dr. Lloyd J. Roth and is staffed by a trained organic chemist who has had special experience with isotopes. These facilities are also used in the training of pharmacologists and in the preparation of labeled drugs.

To date a number of C-14 labeled drugs have already been synthesized in this laboratory. Among these are Isoniazid, para-Aminosalicylic acid, and Diamox acetazoleamide; the last-named drug was also labeled with Sulphur 35 (23). These drugs are used not only in the department of Pharmacology but also in cooperative research projects with physicians in the University of Chicago Clinics.

Studies utilizing both ring and carboxyl-labeled paraaminosalicylic acid have indicated that the drug penetrates the caseous material in concentrations adequate to explain its bacteriostatic action, based on in vitro studies (24). The same ability to penetrate the caseous material was found with Isoniazid (25, 26); this latter drug, however, tends to be retained in the lesion while PAS concentration follows that of the bloodstream.

In addition, by means of autoradiographic techniques, Roth and associates demonstrated that Isoniazid is taken up differentially by such anatomically discrete areas of the brain as the hippocampus and the caudate nucleus (27). The differential uptake of this drug by the forementioned areas of the brain is an intrinsic property of the cells in these structures and is not correlated with the blood supply. This fact was conclusively proved by densitometric measurements of radioautograms prepared after intravenous administration of I^{131}-labeled serum albumin in perfused and non-perfused cat brain (28).

Sulfur-35-labeled carbon disulfide, shown by Richter to effect specific lesions of the globus pallidus and substantia nigra, was found by radioautography to localize most abundantly in the myelin-containing areas of the brain, such as cerebral white matter. It is of interest to note that the content of myelin in the globus pallidus is greater than in other nuclear structures.

Studies are currently in progress on the central nervous system distribution and metabolism of S^{35}-labeled Diamox, C^{14}-labeled phenobarbital and Dilantin sodium.

Counter-measures Against Radiation Injuries

Although a great deal of work has been done on the biochemical and physiological effects of radiation, the mechanisms responsible for acute and chronic radiation injury are largely unknown (29, 30). Similarly many attempts have been made to counteract the effects of ionizing radiations by pre- and post-treatment with drugs and chemical agents. Thus far these efforts have met with limited success. However, several sulfur-containing compounds such as cysteine and mercaptethylamine, a decarboxylated product of cysteine, have shown promise prophylactically and have provided a starting point for further developments in the treatment of radiation injury. There still remains a great deal of research to do on the mode of action and therapy of radiation injury. Therapeutic counter measures in case of disaster, such as an atomic explosion—either accidental or planned, must be devised so as to permit

their use on very large numbers of the population if this ever becomes necessary.

Fundamental knowledge of the nature of radiation damage and its treatment could furnish the key to a clearer understanding of both normal and abnormal cell division and multiplication.

Injurious Effects of Chronic Exposure to Gamma and Neuron Irradiation

During the past few years several studies on the injurious effects of chronic exposure to gamma and neutron irradiation have been conducted in various laboratories (31, 32, 33). However, most of these studies were not concerned with dosage levels in the range which are expected to occur in the vicinity of nuclear reactors. Further information is, therefore, needed on the effects of low doses of gamma and neutron irradiation on experimental animals in order to estimate the hazards associated with occupational exposure to nuclear reactors. Isotopes are proving useful for this type of radiation research. Thus, cobalt 60, a gamma emitter with a half-life of 5 years, is used for studying the biological effects of gamma radiation and polonium-beryllium provides a source of fast neutrons.

In the Air Force Radiation Laboratory at the University of Chicago a study of the effects of repeated exposure to low doses of gamma and neutron irradiation is being conducted on about 4,000 mice by Dr. John Doull and associates. The aim of this research program is to determine the amount of shortening of the life-span and the incidence of leukemia which results from exposure to various low doses of gamma and neutron irradiation. Data of this type will aid in estimating the dangers associated with occupational exposures to radiation from nuclear reactors (34).

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Investigative and Diagnostic Aspects of Exfoliative Cytology[1]

By GEORGE N. PAPANICOLAOU[2], PH.D., M.D.

DR. Rhoads, Dr. Kimbrough, Fellows of the College of Physicians of Philadelphia, and Guests.

I wish to express my sincere appreciation to the Committee on the Alvarenga Prize and the Council of the College of Physicians of Philadelphia for having selected me as a recipient of this highly prized award, which honors the memory of a man, who so ably upheld the noble traditions of the medical profession, Doctor Alvarenga.

I accept it gratefully as a very distinctive honor not only for myself, but also in behalf of my Colleagues and associates, whose collaboration and aid have been of inestimable value to me, and in behalf of the Cornell University Medical College, where, throughout the long period of 43 years, I have enjoyed the blessings of a warm and stimulating environment and of whole-hearted encouragement and support.

The opportunity afforded to me, on this occasion, to be here with you today and to deliver this lecture before such a distinguished audience in this historical hall is a real privilege, which I value greatly.

The study of cells exfoliated from the epithelial lining of various organs of the body dates back to the early 19th Century, when the introduction and expanding use of the compound microscope marked the beginning of an era of intensive cytologic research. The earliest reference to a microscopic examination of a body fluid is presumably that of Donné in 1838, who examined smears of human colostrum. This was a year of historical significance for cytology, for it was in 1838 that Schleiden laid the foundation of the "cell theory", which one year later found a more elaborate and mature expression in Schwann's epoch-making investigations on the structural and growth similarity in animals and plants.

Observations on exfoliated cells or tissue fragments were reported in sputum in 1843, by Walsche, and later in 1858, 1860, and 1875, by Lancereaux, Beale and Hampeln; in urine in 1864, by Sanders; and in exudates by Luecke and Krebs in 1867, and by Quincke in 1875. All these early observations were made by microscopic examination of fresh specimens.

With the development of more adequate techniques for fixation, centrifugation and staining, toward the end of the 19th and the early years of the 20th Centuries, the microscopic examination of body fluids for the diagnosis of cancer and other pathologic conditions gained favor with many pathologists, who began to use it in their laboratories as an accessory diagnostic procedure, particularly in sputum and exudates. It is rather surprising that, despite the enthusiastic support given to it by a number of prominent investigators, the dependability, practical usefulness and great potential value of this diagnostic approach did not receive wider recognition.

This may have been partly due to the fact that, since 1895, when Bahrenberg described a technic for embedding sediments from centrifugated fluid specimens and sectioning them for examination, this so-called cell-block method achieved great popularity among pathologists. No wonder then that such a technic, so similar in every respect to the standard methods used in pathology labora-

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tories for the study of tissue specimens, grew to be a sharp competitor and finally achieved the upper-hand over the technic based on the preparation and evaluation of smears. The use of the latter procedure involved special study and long experience. It is now generally recognized that anyone, even a qualified pathologist, desiring to become an expert in cytologic diagnosis cannot attain this end without receiving special instruction and training for a period of several months, not to mention the even longer time needed for acquiring the necessary experience.

Other serious drawbacks in the approbation and wider acceptance of the cyto-diagnostic method in those years were the lack of relatively simple and adequate techniques for the preparation, fixation, and staining of smears and the rather incomplete knowledge of the normal cellular patterns of the various body fluids. Normal exfoliative cytology has been studied more thoroughly with the aid of improved technical procedures only in recent years, originally in the organs of the female genital tract in the course of studies entirely unrelated to the diagnosis of cancer.

The earliest reference on cytologic examination of secretions from the female genital tract is that of Pouchet in 1847, who studied vaginal smears from normally menstruating women in search of evidence of a spontaneous ovulatory process, which was still disputed in those days. It is rather surprising that for over 80 years, i. e. until 1928, when my preliminary note on the possibility of diagnosing cancer of the uterus by the microscopic examination of vaginal smears was published, this point had been practically ignored.

In attempting to evaluate the factors which have contributed to the more recent growth and widespread use of exfoliative cytology, it might be pertinent to go back briefly to the investigative work begun some 40 years ago on the basic morphology of the cyclic changes in the reproductive organs of the guinea pig. It was in the course of this investigation, which was carried out by the late Professor Charles R. Stockard and myself, that the vaginal smear was introduced as a means of identifying the various stages of the female sex cycle. With the aid of this rather simple smear technic and with improved methods of fixation and staining, it became possible to establish the existence of distinct cytologic patterns appearing in the vaginal secretion in an orderly and rhythmic fashion.

A simple test was thus brought to light, that made possible the accurate determination of the time of ovulation and a better correlation of the morphologic and physiologic changes occurring periodically in the reproductive organs of the guinea pig. Many significant observations and discoveries, such as the isolation of the estrogenic hormone, were made with the aid of this same smear technic, which soon found general use in the study of the reproductive and endocrine functions of a number of lower and higher mammals, including primates. Its subsequent application in women threw new light on the correlation of the ovarian and uterine changes during the various phases of the normal menstrual cycle and on their dependence upon the hypophyseal and other hormonal secretions. The vaginal smear has also proved to be a most serviceable tool in the study of problems related to amenorrhea, sterility, and menopause.

It was during this most productive period that I enjoyed the privilege of a close association with a former recipient of the Alvarenga Prize, the late distinguished endocrinologist, Ephraim Shorr. The demonstration—which was indeed an exciting experience for us—that the administration of an estrogenic preparation would invariably change the atrophic postmenopausal vaginal smear pattern to that characteristic of a young, normally menstruating woman has provided a useful and dependable objective test for assaying estrogenic preparations and appraising their physiologic and therapeutic action in women.

Before proceeding with the discussion of the usefulness of the cytologic method in the diagnosis of cancer, it might be relevant to

make a few remarks here on the nature and general significance of the process of exfoliation upon which this method is based. Exfoliation is the manifestation of a fundamental biological principle which finds its most typical expression in the epithelial tissues, i. e. the skin, which forms a protective sheath over our body and the mucous membrane that line all body cavities. These tissues, because of their exposure to the action of extraneous factors, are subjected to an extensive shedding of their superficially located cells. As these cells are lost, their places are promptly taken by new cells growing from the undifferentiated basal layer of the epithelium, which is endowed with an inherent high potentiality for proliferation and growth.

Epithelial cells exfoliating within the cavities of various organs, such as the vagina, uterus, lung, esophagus, stomach, sigmoid colon, urinary bladder, and others, may be detected and studied microscopically in properly fixed and stained smears prepared from fluid aspirated from these cavities. If the smears are fixed immediately, the cells, though they may be dead or partially degenerated, will retain their structural characteristics to a degree permitting their identification as to origin and type.

The microscopic study of these exfoliated cells, which are actually waste epithelial elements, has grown to such an extent in the past few years as to reach the status of an autonomous branch of the cytologic sciences, known under the recently coined term, "Exfoliative Cytology". Its general significance has been greatly enhanced by its useful application in the diagnosis of malignant disease.

It is a known fact that all carcinomas have their inception within the epithelial lining of the various organs of the body, and, as such, are subjected to the same fundamental biological laws which govern the proliferation, growth and exfoliation processes peculiar to the epithelial tissues. Thus a carcinoma developing within the lining epithelium of an organ continuously throws off some of its superficial cells. Should this be a carcinoma of the uterine cervix, no matter how small, even if it were so small as to be invisible to the naked eye, it would shed some of its superficial cells into the cervical canal. This shedding might occur at a rate far exceeding that of the normal cervical epithelium, since cancer cells are known to multiply and grow much faster than their normal counterparts. By examining microscopically a smear prepared from fluid aspirated from the vagina or the cervical canal, one would thus be able to detect cells derived from a cancerous area and identify them with the aid of morphologic criteria, by which their malignant nature can be ascertained. As a result, a carcinoma of the cervix can be diagnosed by the smear method at a very early stage, prior to invasion and also prior to the appearance of any symptoms. At this point, cancer is still a localized lesion and can be removed by surgery or destroyed by irradiation with very good chances for a complete cure.

The possibilities of using the vaginal smear in the diagnosis of uterine cancer became gradually apparent in the years following 1923, during the course of an exploratory project carried out in cooperation with the Woman's Hospital of New York City. This project was a study of the cytology of the vaginal secretion, first in normal women and then in patients with various pathologic conditions of the uterus, including benign and malignant neoplasms. It was soon realized that malignant cells exfoliated from a carcinoma of the cervix could be reliably differentiated from non-malignant cells by their striking structural abnormalities. The enlargement and deep staining of the nuclei of the malignant cells cause them to be particularly conspicuous. No one could possibly fail to be impressed when seeing them for the first time.

These early studies were reported in 1928, in a brief preliminary paper, which, however, was received with extreme skepticism. The morphologic soundness of the method has never been questioned but its practical value and

dependability as a diagnostic procedure were looked upon with much distrust. Moreover, since the uterine cervix was accessible to exploration by biopsy, the use of the cytologic examination of vaginal smears appeared to be superfluous.

The turning point in the attitude of medical men toward the use of the cytologic method in cancer diagnosis came about in 1943, when the results of a more exhaustive study, on the value of the vaginal smear in the diagnosis of cancer of the uterus, carried out at the Department of Gynecology of Cornell University Medical College and the Lying-In Hospital, were published in a monograph by Herbert F. Traut and me. These observations were soon confirmed, and the method was endorsed by Joe V. Meigs, Ruth M. Graham, Maurice Fremont-Smith and associates of the Harvard Medical School and the Vincent Memorial Hospital in Boston in 1943, and by Theodore Neustaedter and Locke L. Mackenzie of the New York Post-Graduate Medical School in 1944.

Since then the cytologic method has found general application in the diagnosis not only of malignant lesions of the uterus but also of several other organs of the body. During the past 13 years, many significant contributions have been made in this rapidly growing field. The sanction given to this diagnostic approach by the College of American Pathologists and the American Society of Clinical Pathologists has greatly contributed to its universal recognition and has paved the way for its introduction into numerous pathology laboratories here and abroad. With the cooperation of these two societies of pathologists, the International Union Against Cancer and the Inter-Society Cytology Council, an international conference centering on Cytology was held in Chicago last Fall. Its success was so overwhelming that a second International Congress is now scheduled to take place this Summer in Europe, where investigative work in this new field is being pursued very actively in many hospitals and university clinics.

Perhaps the most successful application of the smear technic has been in the diagnosis of cancer of the cervix. The relative ease with which material for a cytologic examination can be obtained from this organ has undoubtedly been the major factor for the unusually rapid advancement of our knowledge in the exfoliative cytology and histopathology of carcinomas of the uterine cervix. Progress has been most notable in the study of early malignant lesions brought to light by the examination of vaginal and cervical smears. The great number of intra-epithelial carcinomas or carcinomas-in-situ thus far uncovered has provided the pathologists with excellent material for the study of the histogenesis of cervical carcinoma, and the clinician with the opportunity to attack cancer more efficiently at an early curable stage.

In the early preinvasive stage of cancer, the morphologic changes characteristic of malignancy are almost entirely confined to the nucleus and consist chiefly in its disproportionate enlargement and a deeper staining of its chromatin content, known as hyperchromasia. The cells, as a whole, may still retain, to a large extent, their similarity to normal cervical cells, whereas those of the advanced, invasive carcinoma exhibit markedly abnormal and bizarre forms differing greatly from all normal types.

On the basis of the differences in the structural characteristics of cells exfoliating from cervical carcinomas it is often possible to recognize not only the presence of a malignant lesion but also its type and its developmental stage. In addition, it appears that some of the cytologic patterns may even possess a certain prognostic significance. For example, the predominance of abnormal cells of the superficial squamous type in the smears, suggests a decidedly more favorable prognosis than the presence of deeper squamous or parabasal cells or of cells of the endocervical type. In cases with a smear pattern of the superficial squamous type the lesion may sometimes undergo regression, whereas in the other two

types it usually follows a progressive course. It is evident that, as our knowledge increases, the frontiers of our research will extend more and more into the vast realm of early malignant and premalignant or potentially malignant lesions, the nature of which is still obscure. The clarification of these baffling and elusive borderline cases poses a most provocative challenge for both cytologists and pathologists.

The normal and malignant exfoliative cytology of the endometrium has not thus far been as thoroughly explored as that of the cervix. Endometrial cells are seldom found in vaginal or even cervical smears except in the presence of uterine bleeding. In adenocarcinomas with a concomitant cervical infection a contingent obstruction of the endocervical canal may prevent the passage of exfoliated malignant endometrial cells into the vagina. Direct aspiration of fluid from the uterine cavity, whenever possible, would, of course, provide more adequate material for cytologic study. Such a procedure can be performed with relative ease, with the aid of a thin, flexible, metal cannula. This is now being done by a fair number of gynecologists not only selectively, in cases with suspicious uterine bleeding, but also routinely. The diagnostic accuracy of fundal adenocarcinomas which has never been fully satisfactory on the basis of vaginal smears alone, can be markedly improved with the use of adequately prepared endometrial smears. The chance of detecting uterine adenocarcinomas at an early stage is also much greater in endometrial aspiration than in vaginal or cervical smears.

Occasionally cells exfoliated from adenocarcinomas of the tubes or the ovaries may reach the uterine cavity or even the vagina. There are several cases on record of carcinomas of these organs being detected primarily by the examination of vaginal or endometrial smears. However, the application of this method to these organs is of value chiefly in cases in which cytologic findings are conclusively positive.

In the past ten years, the cytologic method has been applied at a steadily increasing rate in the diagnosis of cancer not only of the uterus but also of several other organs of the body. Its use has thus far been found to be more effective in the diagnosis of cancer of the lung, urinary bladder, esophagus, stomach, rectum and sigmoid colon and the pleural and peritoneal cavities. In all these organs extensive tests have shown it to be a valuable adjunct to biopsy and other established procedures for the diagnosis of cancer. Many unsuspected carcinomas have been detected by this method, some at a very early stage.

In the respiratory tract cytologic examination of either sputum or bronchial washings has proved to be equally satisfactory. In the lung, as in other organs, primary carcinomas can be diagnosed more readily than metastatic lesions. The latter often fails to shed cells into the lumen of the bronchial tree.

In the gastro-intestinal tract very good results have been obtained in the diagnosis of carcinomas of the stomach, the esophagus and the rectum. For obtaining material from the stomach several special techniques are in use, such as the gastric balloon and brush techniques and the chymotrypsin method of Rubin. Washings from the esophagus and the rectum provide cytologic material from these two organs.

In the urinary and male genital tract the method is of particular value in cases of papillary and other tumors developing in the transitional epithelium of the urinary bladder and the pelvis of the kidney. Smears are prepared from the sediment of centrifugated urine obtained from the bladder or the kidney pelvis. Intramural carcinomas of the kidney can be diagnosed only when the tumor breaks through the epithelium of the urinary passages. For the exploration of the prostate, the examination of urine specimens alone proved to be unsatisfactory, but much better results have been reported with smears prepared from secretion squeezed out of the prostate by gentle massage. Several hidden carcinomas of the

prostate have been uncovered when such secretion was available.

In pleural, peritoneal and pericardial exudates, and in fluids aspirated from other body cavities or cysts, the exfoliating cells may provide evidence of a primary or metastatic malignant lesion. Exfoliated malignant cells found in exudates are often very numerous and may exhibit extremely active proliferation and growth due to the particularly favorable nutritive environment provided by the exudates.

Although the earliest reference to a microscopic examination of a body fluid was, as stated above, on breast secretion, the use of the cytologic method in the diagnosis of cancer of the breast has thus far been very limited. The main reason for this is perhaps the difficulty in obtaining secretion from the breast except during lactation and in late pregnancy. However, in cases in which secretion is spontaneous or induced by gentle palpation or with the aid of a hand breast pump, the results have been most satisfactory, especially in the diagnosis of papillomas or papillary carcinomas developing in the large ducts of the mammary gland. The early appearance of exfoliation in such cases enhances the diagnostic value of the method since it makes possible the detection of incipient malignant lesions prior to the appearance of a palpable mass or to the lymph node involvement. Several unsuspected carcinomas-in-situ or very early ductal carcinomas of the breast uncovered by the routine examination of breast secretion are already on record.

In attempting to evaluate the diagnostic accuracy of the cytologic method in all its applications one should bear in mind that positive findings always carry greater weight than negative. When cancer cells are present in a smear the cytologist feels more confident in the validity of his observation than when such cells are absent. Positive cytologic reports rendered by adequately trained and experienced cytologists and cytopathologists show indeed a high degree of accuracy. On the other hand, negative findings tend to be less reliable. One should, therefore, never lose sight of the fact that a negative cytologic report provides no guaranty against the presence of cancer.

The accuracy of negative reports varies greatly, being lower in organs from which suitable material cannot be easily procured, such as in the kidney, prostate and breast, than in other more accessible organs like the uterine cervix, in which the degree of accuracy reaches a much higher level. Other factors such as the number of available specimens and their proper preservation and staining may also affect the diagnostic results appreciably. In cancer of the lung for instance, it has been shown that the accuracy of the cytologic examination of sputum can be raised from an average of 71% with only one specimen to over 90% with the examination of five specimens.

Positive cytologic findings should, of course, be confirmed by a biopsy whenever possible. However, there are instances where such confirmation is not feasible. There are also cases on record of early carcinoma of the cervix revealed by a cytologic examination in which the biopsy or even repeated biopsies were negative. When faced with such conflicting reports the surgeon finds himself in a dilemma as to whether he should proceed with an operation without pathologic confirmation or ignore the positive cytologic findings—a rather hazardous decision since it might ultimately prove detrimental or even fatal to the patient. In earlier years this issue was one of cytology versus pathology but in more recent times it has been gradually changing to one of positive versus negative findings. It is now generally conceded that in a case of a small intraepithelial lesion of the cervix, a single or even a multiple biopsy may sometimes be negative and, therefore, should not invalidate a well documented positive cytology.

The utilization of the cytologic method, as developed in the aforementioned studies, has greatly stimulated research in various fields of Biology, Biochemistry, and Medicine. By virtue of its great simplicity and its unique feature of permitting day by day observations

without the need of surgical intervention, this method has provided an excellent tool for many new experimental and clinical investigations. The early appearance of malignant changes and their progressive or regressive course in spontaneous or experimentally induced tumors, the results of operative procedures, and the action and effects of various drugs and other modes of therapy, such as radiation, are only a few of the problems which have been and are still being actively explored with the aid of this rather simple technic.

The most serious obstacle to the wider utilization of Exfoliative Cytology as a cancer control measure has thus far been the insufficiency of existing laboratory facilities for handling efficiently the large amount of cytologic material necessary for the screening of large segments of the population. There is still a great shortage of doctors and cytotechnologists with adequate training in this type of work, though their number has been growing steadily. A more rapid increase may now be anticipated as a result of new plans initiated by the Public Health Service and the American Cancer Society for a more active campaign to encourage and support special education in this field.

The feasibility of mass screening for the purpose of detecting covert and asymptomatic carcinomas of the uterine cervix has been convincingly proved by the pilot screening project carried out in Memphis, Tennessee, by the University of Tennessee and the National Cancer Institute. Of the 108,000 women included in this test, 393 were found to harbor intraepithelial and 373 invasive carcinomas of the uterus, a total of 766, i. e. approximately 7 per 1,000. Of the 393 intraepithelial carcinomas 90%, and of the 373 invasive 30%, were unsuspected. These results show clearly the value of the cytologic method for the early detection of cancer. Similar mass screening projects are now in progress in other states under the auspices of the Public Health Service and the American Cancer Society. Thus the prospect of large scale screening programs that might gradually be extended to include all women of cancer age—a thought that would have been disposed of as a utopia only a few years ago—is now becoming a subject of rational speculation. Even if this goal is not fully realized its zealous pursuance will go a long way toward the control and eventual eradication of a disease unequalled in cruelty and greed.

Public Health in Pennsylvania: Department of Health, Plans and Programs[1]

By J. THOMAS MILLINGTON[2], M.D., M.P.H.

IT IS a pleasure for me to be at this joint meeting of the Section on Preventive Medicine of the College of Physicians of Philadelphia and Region I of the Pennsylvania Public Health Association, and to present a part of the Second Arthur Parker Hitchens Lecture. When I was asked to talk tonight, one of the reasons stated was that I had been close to Colonel Hitchens during the time he served in Philadelphia. Since that letter came, I have been thinking about that scholastic year at the University of Pennsylvania. I can recall the day I enrolled, the shock of meeting a former classmate of mine at Jefferson Medical College, who was rehabilitating because of tuberculosis; the gradual change in attitude of the students as we progressed into postgraduate methods of study; the use of seminars; the attempt to inculcate the value of group discussion; the field trips; the habit of taking time out for tea and cookies in the midafternoon.

All of these experiences were set against the background of the happenings in Europe during that eventful fall of 1939.

But as I recall them, I do not actually believe that any members of that first class could have been considered "close" to Colonel Hitchens. Remember, too, that this was a new and startling program for the Commonwealth of Pennsylvania: postgraduate training in Public Health, so that the administrator of that program was not always available for meetings with the students. I believe we were then, as students usually are, much closer to members of the teaching staff than we were to the head of the school. Most of us have since found that administrators do not always have as much time to meet and talk with as many of the persons, who think they should be able to discuss their problems, as the administrator would wish. Opening the door to an office can't put more hours into the day.

I have had some difficulty preparing this lecture. One always does when given a subject as broad as this one—*Department of Health: Plans and Programs*. How many times have these nonspecific titles created confusion? No one has any way of knowing what words like 'Public Health' mean to other individuals. All of you can recall being asked to, "just say something about public health", and appearing at a meeting as an ardent missionary of the cause and expounding on the value of preventing disease, disability, and death by organized community efforts to an audience that was patiently waiting for you to finish so they could get down to the real reason why you had been asked to be present. The "how come, and why don't you, and how can they get away with", session. The period when the things the people recognized as needs were expressed; when you were told in no uncertain terms what local needs and problems were. Chronic diseases and their effect upon the community are relatively unimportant to a group who ask: "why don't you make these industrial plants keep their waste products out of the air?," or, "why do our children have to attend classes in damp cellars in our school buildings?," "how can we get sanitary sewers into a rural township at little or no expense to the township?", or explain how immunization programs in well child conferences can be anything but "socialized medicine".

But tonight, I am sure that everyone will

[1] Arthur Parker Hitchens Lecture IIa, College of Physicians of Philadelphia, 5 March 1957.

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realize the scope of problems in public health and not be disappointed if we don't mention what we are considering in the particular field in which you are interested. It always has been hard to talk about the broad subject of public health, even when the definition of public health had some limitations, but now we are trying to find out "where we are going and how we are doing in Public Health." Since the Task Force Report has been published, any one who attempts to talk on "Public Health in Pennsylvania" should make arrangements to do it as a member of a panel; with representatives from the State Departments of Welfare, Public Assistance, Public Instruction, the Budget Office, and a Deputy Attorney General sitting right alongside of him.

In considering a way to approach this topic, I decided to use as a text the phrase from the invitation to speak—"to set the stage," as this could delineate an area which might be examined. The need for setting the stage has been brought out in some of our correspondence and phone calls during recent weeks, which have contained these questions: "How long does it take you in Pennsylvania to?" "Why doesn't the medical profession get on the ball and do as they are doing in Connecticut?" "Why can they have this program in the county next door?" "Do you mean to tell me a program approved on the State level can be stopped in our county?"

As an administrator, I then passed these same questions on to our program directors with an additional question—"Do you think we should have programs to supply these services, and what do you need most to be able to develop these programs?" Their answers to these questions have been used as a basis for this talk—"Setting the Stage." From the point of view of a program director, Maternal and Child Health, Tuberculosis Control, Communicable Disease Control, etc., how can you imagine the scene in which the activities they are planning or which they think desirable will take place?, as a site of public health activities how would you describe Pennsylvania?

If we could use some of the new tricks of television and approach it from a distance and see it as a whole, we would be impressed first by its size. As one of our new program directors phrased it, "My God, Pennsylvania is big." Big in area, in distances from place to place. Big in the number of people who live here, over eleven million people. If we had to consider it as just *one* community with eleven million residents, it would be a complex problem.

But by using this new technique we approach this mass and come close enough to see that it isn't one community, but is arranged into a number of varying-sized and shaped geographic patterns called counties. There are 67 of them. Some of the large geographic areas have only a few people in them, and some of the smaller counties have vast numbers of people living in them. If we can come down still closer we find 2,563 municipalities located in these counties.

Having examined this setting, what would be our decision about how to make the most efficient use of it? If we were using it for a theatrical production, we would say that a stage—huge and barren enough to hold a cast of the relative size of our population is unrealistic, ungainly, and impossible for effective direction. We would also want to avoid a number of sets that were too small for the range of our production. For every endeavor there is a setting which is most efficient for the needed purpose.

These same principles apply to public health programs. The State is too large, and the number of small communities too great, for efficiency. Therefore, you will not be surprised to hear that the first item the program directors listed in answer to my question, "What is your first need?" was: local health units capable of studying local needs and problems, and planning, and carrying out programs designed to meet their specific needs.

You know that the problem of stimulating the recognition of the need for, and encouraging the development of, local health units has been given top priority by every organization

interested in Public Health in Pennsylvania. The result of their efforts to date are five units specifically designed to meet the needs of the people who live in these areas: Philadelphia, and the county units of Butler, Bucks, Erie, and Allegheny. There are four counties in which a referendum or resolution may occur within a year or so: Lehigh, Montgomery, York, and Lancaster. Eleven counties have evidenced positive interest and are in the process of completing or starting surveys. There are nine counties in which some interest is apparent, and 38 counties in which there is no interest at all. Perhaps we should be satisfied that in the last six years the number of county health departments has increased 500%. We are encouraged by the formation of these county units and hopeful that the activity in the nine other counties will in the near future mean other well-staffed local health departments providing community promotion of programs to cope with their own problems; flexible programs organized and planned locally to meet ever changing local needs. To repeat —the basic need of the State preventable disease programs is local health units. Decentralization of State Health Services into well staffed Regions is a step in solving this need, but a Regional Office of the State Department of Health can never be a substitute for a county health department. Until we have these county departments, the preventable disease services must be limited to direct services in the vast areas of the State. In many of the programs we are so busy fighting the fires of present problems, we can't get to the job of finding out how to prevent them.

But we have not been waiting for these changes or just confining our activities to those programs and services which had been traditional with the State Department of Health. Each Division and Section has been reviewing the needs of the people of Pennsylvania in the specific area of public health for which they had been given responsibility. Some of this study has resulted in new programs already underway; some of the studies have not yet been translated into direct services. Tonight I will report on just a few of them.

DENTAL HEALTH

Dental caries is numerically the most common physical defect found in man. So prevalent is this defect that we have been criticized for including the school dentist in the plans for the school health program. We should emphasize that dental health programs are established on the same basis, follow the same patterns, and have the same goal as all other public health programs: the prevention of disease and deformity and the restoration of normal function to the child handicapped by a dentofacial defect.

We have had and continue to have case-finding programs chiefly in the school; corrective programs which are cooperative, a local sponsoring agent supplies equipment and facilities and the State Health Department pays the dental clinician. These are basically demonstration programs, but also supply direct dental service to children. At one time, 125 clinics were in operation. We are now cooperating in 98, and in 26 communities the services have been continued after the State help was withdrawn. We have had and continue to have programs to prevent dental defects; 68 communities with a total population of 3,300,000 are now providing fluoridated water. This is about 37% of the total population using public water supply. Seventy-three communities are providing topical applications for some of their elementary school children.

One new program is being studied and a plan developed to activate it. This is to determine the need for service and the method of supplying that service, dental care, in home bound children. We have activated a plan to provide dental care by using hospital facilities for the child with cerebral palsy. This plan includes training courses for dentists who will provide the specialized care these children require. A third program which will start shortly will be a demonstration of the use of a school and the

school water supply as a method of securing reduction in incidence of dental caries in areas where public water supplies are not available.

We have this year started a service for children with dentofacial handicaps not associated with cleft lip and/or cleft palate. The purpose of this program is to provide treatment for a child with one or more of the following dentofacial handicaps which constitutes a handicap of such magnitude as to require essential rehabilitation, that is, one where because of the nature of the handicap, the health and future of the child may be in jeopardy, because the appearance of the child is marred, and speech impairment, emotional and social maladjustment is present. The dentofacial deformities are: (a) underdeveloped lower jaw, facial asymmetry, or protruding teeth; (b) malformation or mutilation of the oral structures which disturb such functions as speech, chewing, swallowing, or sucking; (c) loss or absence of teeth sufficient to constitute a present or potential health problem. Up to the present time we have received applications for 32 children; 10 cases are under treatment, and treatment will probably be started on 10 more in this fiscal year.

COMMUNICABLE DISEASE CONTROL

The activities of this Division can be well described in two words: *Poliomyelitis Vaccine.* From the early days of 1954 until the present, the problems of handling this one product have kept us all busy. It also is a good example of how the best laid plans of mice and men are changed by circumstances beyond their control.

To start with, all we had to do was find out how to take a sum of money that would provide protection for one-third of the children in the State and give protection to every child. Our plan was to use the existing pattern of medical services—where most people, some 80%, go to their family doctor and 20% are provided service from clinics. We would provide, cooperatively, immunization to all children and then retire from the polio vaccine program, and permit the polio vaccine to become a normal part of the immunization program. This was the plan. But outside forces have altered the original concept, until the entire population under 50 is now the goal, and legislation has been introduced to change the School Code to include poliomyelitis vaccine. Let us consider this proposal as part of a plan.

It is the duty of the Department of Health to protect the health of the people of this Commonwealth and to determine and employ the most efficient and practical means for the prevention and suppression of disease. We have studied the proposed legislation to require immunization against poliomyelitis as a prerequisite for school attendance against this background of our mandated duty and our experience with other immunization procedures.

Prevention of disease is the ideal goal. We have in diphtheria an example of a disease for which we had a specific treatment—antitoxin, for 20 years, without making much impact upon the number of people dying every year from this disease. However, as soon as we found a way to prevent the disease, we started a drastic reduction in the number of deaths —from 1,983 deaths in 1921, to 364 in 1931, to a low of 1 death in 1956. Prevention of disease reduces mortality much more drastically than treatment of disease.

It is the practice in Pennsylvania to immunize against four diseases: smallpox, diphtheria, tetanus, whooping cough. Now poliomyelitis has been added to this list. Under existing statutes, only protection against smallpox is compulsory. It is proposed that immunization against poliomyelitis should be made compulsory. The Department of Health suggests that if legislation is passed to make immunization against poliomyelitis compulsory, it would be well to make immunization against diphtheria and tetanus compulsory as well. We do not usually favor compulsion, but we must approve of any measure which will provide protection against disease to more

people. Our experience indicates that, without compulsion, we do not achieve our goal of complete protection against specific diseases. By requiring vaccination against smallpox, we have 100% of the population over school age immunized. We recognize that there is a weakness in the present requirements in that 50% to 60% of parents wait until just before school attendance is mandatory before having the child vaccinated against smallpox.

We do not require immunization against diphtheria and tetanus. Surveys to determine the number of children protected against these diseases show that we do not have a uniform level of protection against them. In some counties which have active public health programs, we still have 25% of the children not protected against these diseases. In other counties without active public health programs, 60% of the children have not been protected. In some school districts where interest of the parents and active programs do exist, over 90% of the children enrolled have been protected. Actual figures compiled from school medical examination forms indicate that for the children reported, at least 50% of the school population is not protected against these two diseases.

Furthermore, recent epidemics of diphtheria across the nation demonstrate that in areas without a high level of protection, diphtheria can and will again occur as an epidemic disease. Immunization programs must be continuous. These reports would indicate that if our goal is to protect all our children against these diseases, the voluntary method does not work. We not only have children sick with these diseases, but we have children die with them as well.

Our experience in two voluntary free polio vaccine programs—one state-wide in 1955—indicates that immunization will not be accepted by all persons: 15% in 1955 refused free vaccine. This was the first use of the vaccine and people were not yet convinced of its safety. But in 1957, after 50 million doses of vaccine had been used and its safety demonstrated, 11% refused free vaccine in some of our best and most cooperative areas. After the intensive educational programs about the use of the vaccine have been considered, I believe we must expect that, in the near future, as soon as the campaigns stop and poliomyelitis vaccination becomes a part of normal practice, the number of children unprotected against poliomyelitis will soon equal the number now not protected against diphtheria and tetanus.

Deaths Occurring in Pennsylvania from Diphtheria, Tetanus, & Poliomyelitis

1950–1955

Year	Tetanus	Diphtheria	Poliomyelitis
1950	9	9	162
1951	10	13	41
1952	5	7	144
1953	9	6	58
1954	4	2	49
1955	9	4	21
1956	10	1	11

Protection against tetanus is recommended by Civil Defense authorities as an added precaution against the risks of natural and enemy disaster. Because of the danger of this frequently fatal illness following a wound of any kind, tetanus toxoid affords valuable protection in either instance.

We would continue to urge that poliomyelitis be added to the list of diseases against which we are now trying to have parents start protection by immunization when the child is two or three months old, and not to have parents wait until children are of school age before protecting them against poliomyelitis and these other diseases

MATERNAL AND CHILD HEALTH

This Division has been one of our most active during recent years. The list of programs which started with the Well Child Conferences for the guidance and development of the normal infant and child had been expanded to include the child handicapped with rheumatic fever, and then the child with cleft palate and harelip, and other defects requiring plastic surgery, and the mandated school medical

examination program. We have maintained the basic concept of service to the child but have provided more services to these children.

Over the years we have broadened our concept of the crippled child from that of the child who cannot walk or run normally, to include any child who has a condition which prevents him from growing and developing to his fullest potential. We have held training programs on the growth and development of the normal child. Because the handicapped child is to start with a child in a family we have widened the scope of our services to include the pediatrician, the social worker, the nutritionist, as well as the orthopedic specialist and physical therapist. For the children who have attended our orthopedic diagnostic clinics we are developing a program of more frequent clinics. Heart disease in children now includes the child with congenital defects as well as rheumatic fever.

The program for hard of hearing children is carried on in conjunction with the Department of Public Instruction. Although the Health Department's activity in this area began only in January of this year, already 24 children have received complete examinations and have been fitted with hearing aids.

Almost 1 in 200 persons have some sort of convulsive seizures. How a seizure in a classroom can affect a child's acceptance by his classmates is easily understood. New methods of diagnosis and therapy have been developed which will allow approximately 80% of people with epilepsy to live productive and socially acceptable lives. Much of the knowledge and facilities needed, however, are confined to our larger medical centers. The Department of Health has embarked on a program to bring these facilities within the reach of all children in need in the Commonwealth. The first state-sponsored clinic for children with convulsive disorders was opened in Harrisburg in January, 1957. Others will be developed in different areas of the State.

The Department of Health is extremely proud of a program which, although it serves only a small number of children, meets a tremendous need. Some infants are born without an arm or a leg. Previously artificial limbs were not supplied until the child was in his teens or later. Now as a result of research in this field children below the age of two are being fitted with prosthetic devices and are being trained in their use. In cooperation with the Industrial Home in Pittsburgh, 16 child amputees were fitted with artificial limbs and trained in their use during 1956. The treatment and training these children are receiving will have a very beneficial effect on their future integration in society.

Satisfactory as this progress is, there is still a great deal to be done. Our school program shows that of 720,719 children examined, 248,152 had conditions amenable to treatment. Most of these, of course, were minor. However, the health of our children demands the constant vigilance and effort of us all—both private and public agencies and individuals. We must utilize all the facilities we have available wisely.

The development of special programs for children with different types of medical and surgical conditions, although necessary in the beginning, has probably served its purpose. Further development of special programs will probably mean duplication of services and dissipation of our resources and energy. At the present time, the Department of Health is considering how to integrate its services for handicapped children so that certain basic services will be available to all children regardless of their handicap and specialized services to those who need them. There are two ways in which this can take place. One is to set up giant state clinics for children with all types of handicaps. The other is to strengthen local hospital and health services for children in the different areas. We look forward to developing our program along the latter lines.

These are some of the plans and programs we have been working on. There are others, just as important: the changing concept of tuberculosis control and chemotherapy; the

plans for a Chronic Addictive Disease Hospital; plans in other Divisions—Industrial Hygiene with Radiation Control; Environmental Hygiene; Environmental Safety with its accident control and Emergency Poison Center programs; and plans in Chronic Disease Control which we have left out of this talk because Doctor Scheffey and Doctor Dixon will speak on subjects in this field.

In closing, I would like to suggest that perhaps we have reached the end of the phase of disease control in which public health as the representative of the organized community effort had the most important part to play and that preventive medicine, the control of the health of the individual under the guidance of his family doctor, will become more and more important. As we look back to see that we have used research to find the causes of diseases; how they spread; why they developed in some places and not in others, we found ways to find cases early, to make accurate diagnosis; we found efficient ways of treating cases of disease to prevent spread; we found methods to prevent people from catching disease; we see that disease, being no respecter of nations or races, caused these questions to be asked many times in different countries and with different tongues. Gradually, piece by piece, the answers to these questions were assembled into patterns of practical and efficient means of disease control. Then it was recognized that these various patterns could be arranged into four categories which Mattison has called the physical, physiological, epidemiological, and educational barriers against disease. It is interesting that we have now reached the point where many of these barriers against disease have lost their identity as barriers and have become a part of our pattern of living. Just one of the many things we take for granted from the time we get up until we go to bed at night.

Just think of today as most of us experienced it—sleep in a house which meets minimum housing standards; thermostat clicks on before we get up and we are protected from getting out of bed in a chilly room; the bathroom's environmental sanitation deluxe; for the man who uses a shaving brush, the danger of anthrax eliminated by the manufacturing process; drinking water, filtered, chlorinated, and in some places fluoridated; nutritional needs met by fruit juices; pasteurized milk fortified with Vitamin D, or skim milk for the low fat diet; fortified cereal or even a high protein specialty; fortified bread; your after breakfast cigarette may be a filtered brand; you leave for work and your means of transportation has been inspected to safeguard against accidents (all but the driver); if during the day you eat out, the restaurant has been inspected and licensed, in some places your waiter may have had a chest x-ray; your chances of exposure to disease are decreased by actions of the health department in eliminating vectors; by techniques of isolation and epidemiology—probably you have been immunized against diphtheria, tetanus, and poliomyelitis. You have been vaccinated, whether you wanted it or not, you have been protected. Perhaps the only part of this whole protective pattern which required any initiative by the individual was the poliomyelitis shot.

We, the representatives of the organized community effort, will need and continue to use and find new values and methods of using these tested barriers of disease. They have a place in preventive medicine, and I am sure the doctors, guardians of the health of the individual, will adapt these tools to their needs to provide a united effort, community and individual—protecting our health.

Cancer as a Public Health Problem[1]

By LEWIS C. SCHEFFEY[2], M.D.

THE foremost impact of cancer as a public health problem is, in my opinion, the need to constantly alert the community to the value of early cancer detection and prompt treatment, if prolonged suffering and ultimate death are to be overcome. Even so there will occur discouraging instances in which a lesion apparently amenable to adequate therapy recurs fairly promptly and metastasizes widely because of some biologic quirk or metabolic deviation that defies explanation. On the other hand there is living proof all about us of the result of early and efficacious treatment. Likewise there is an increased trend in requests for periodic health maintenance and so-called cancer detection examinations on the part of the populace. The medical profession is aware of and must be respondent to the positive role that is theirs, not simply with regard to cancer detection *per se*, but to the increasing desire for adequate periodic health maintenance "check-ups."

With the foregoing statement as a base line for discussion, how can the law of supply and demand be met—or to reverse the context how can the medical profession meet this challenge in the community? As I see it, we have many agencies striving to do their part and from various avenues of approach. What must be done is to take advantage of all these channels by thoughtful and practiced coordination, avoiding unnecessary duplication of effort wherever possible. Let me attempt to tell you, in the brief time allotted, of some of the problems confronting us in this respect and of the ways in which capable groups involved are laboring to provide cooperative effort for the benefit of the public and for effective action by the medical profession.

Even since the advent of cellular pathology in Virchow's day, the clinic and the laboratory have been battling cancer from all angles and at all levels, but it was not until the early days of the present century—in 1913—that cancer began to be discussed as a public health problem in the lay press. It was then too that the American Society for the Control of Cancer was organized for the study of cancer, the effort being favorably looked upon by the American Medical Association, the earlier Clinical Congress of Surgeons of North America, the American Gynecological Society, the American Surgical Association, the Association of Pathologists and Bacteriologists, the American Dermatological Association, and the movement progressively motivated other professional and lay groups as well. Progress was modest. Came the days of the "Women's Field Army" in 1936, and finally in 1944 the organization we know as the American Cancer Society, Inc, "the only voluntary national health agency in the United States devoted to the control of cancer through a comprehensive program of *research, education* and *service*".

I have spoken of this group first in order to trace the development of the volunteer organization that has won the confidence of organized medicine, the United States Government and its citizenry, for the financial contributions of the latter have advanced from $10,000 in 1913 to $27,000,000 in 1956, an accomplishment which I am proud to mention in my capacity as current President of the Philadelphia Division.

Integrated with the Cancer Society's activities, as you are doubtless aware, are the American Medical Association, American College of Surgeons and the National Cancer Institute of the Public Health Service. National, state and local public health services contribute their interest and support. Organized medicine at all levels, medical schools, hospitals and the profession at large cooperate with the personnel

[1] Arthur Parker Hitchens Lecture IIb, College of Physicians of Philadelphia, 5 March 1957.

[2] President, College of Physicians of Philadelphia.

of the American Cancer Society units (2,788) far and wide throughout our land, and so do countless lay and semi-professional health groups familiar to many of us. Our own Pennsylvania Cancer Coordinating Committee serves as a near example of what I am attempting to convey. The stage for cancer control is well set, and now I wish to mention some specific facets of this great cooperative effort on behalf of public health, involving research, education and service.

RESEARCH

The imagination and hope of the man in the street is fired by the magical word "research" and rightly so, for it has captured the substantial interest of philanthropic groups and individuals everywhere. The Cancer Society's budget alone in this respect amounted to 30 per cent (about 9 million) during the past year, while the National Cancer Institute's appropriation of 25 million last year was raised to 48 million in 1957. I wish that time permitted me to explain the various research activities to which the funds of both these organizations are channelled, for they run the gamut of fundamental and clinical research, fellowships of all varieties, cancer control programs, and associated activities involving a veritable army of personnel, hoping to advance etiologic, diagnostic and therapeutic knowledge. The responsibility for wise allocation of these funds, as recommended by research advisory committees is grave indeed; the obligation to the people is truly great, for all the money spent comes from the people, through taxation and contributed money.

EDUCATION

Making the public aware of the cancer problem from a practical point of view is, I believe, a harder task than getting funds for research or furnishing service to ill patients. It is a never-ending propaganda campaign, and one would become discouraged were it not for the fact that progress is being made through constantly broadening the avenues of appeal. I would indeed be presumptuous to reiterate to this audience the well-known means of mass communication that use all modern visual and auditory methods to bring the message of early cancer detection to all segments in public life. Suffice to say that these programs are constantly under review and readaptation in the light of increasing knowledge and experience. I might say at this time that the Philadelphia Division was a pioneer in this respect; hence it is well-adapted, and even ahead in some respects, in implementing the national society's recommendations resulting from a comprehensive review of the nationwide public education program. We cannot remain static.

I am indebted to Dr. John B. Dibeler, M.P.H., Educational Director of the Philadelphia Division, for making some of this studied information available to me as follows:

1. Primary emphasis on annual health maintenance examinations rather than simply stressing the "Seven Danger Signals" which already may mean advanced cancer.
2. Annual chest x-rays for all adults, rather than semi-annual ones for men over 45.
3. Pelvic examinations for all adult women, rather than limitation to women over 35, and inclusion of the Papanicolaou cell test.
4. Rectal examinations, both digital and proctoscopic.
5. Continued propaganda for breast self-examination.
6. Selective rather than mass appeals by urging cancer detection examinations as a sound economic policy for protection against illness.
7. Consideration of the factors that cultural, economic and language barriers play in restraining the 40 per cent of the population in one or all of these categories who decline, resent, or are apathetic to health maintenance and cancer detection programs.
8. Greater emphasis on professional education to fortify and stress the role of the family doctor as well as the specialist in health maintenance and cancer detection. In this respect strength will be added to the Society's long-time objective "Every Doctor's Office a Cancer Detection Center."

In considering the educational factor in this discussion the part that concerns the groups already mentioned is self-evident, and in line with my original thesis stressing the need for local cooperative effort. Let me cite but two of many instances as illustrative of the latitude of our thinking. First, the close liaison between the Committee on Cancer Control of the Philadelphia County Medical Society, and the Philadelphia Division of the American Cancer Society; second, a recent announcement by Philadelphia's Health Commissioner, Dr. James P. Dixon stating that more than 200 women employees in the Division of Public Health Services in the Department of Public Health had signed up for a voluntary program of instruction in the technics of breast self-examination!

SERVICE

The service aspects of the cancer problem have to do with less spectacular tasks designed to ameliorate suffering as far as our budget will go. This humane service is geared to the indigent patient particularly and includes dressings, sick-room equipment and supplies. Visiting nurse service has been subsidized to the extent of $25,000 a year and a modest supply of radium is available through the generosity of an individual for qualified physicians to use for indigent patients.

Too much credit cannot be given to the volunteer workers of the Philadelphia Division. Not only do they labor without stint in the campaigns for funds, but their efforts in preparing the dressings alluded to can be better appreciated by stating that in the past year, 400,000 packets served nearly 800 patients! Those who direct the volunteer works do not spare themselves in the great amount of organizational effort entailed. That they merit the confidence of those whom they direct is evidenced by their loyalty and faithful attention to these greatly needed duties. I know full well that I have only skimmed the surface with these brief remarks about the service area of the Society.

In conclusion, from this all too sketchy review of a complex problem, a fundamental fact stands out, viz; early cancer detection can only be accomplished by the examination of more and more people accepting the opportunities afforded them by public health educational programs, and acceptance by more and more members of a medical profession prepared and willing to accept the concept that I repeat again—"Every Doctor's Office a Cancer Detection Center"—with emphasis upon all that this slogan entails.

Progress in Public Health in Philadelphia[1]

By JAMES P. DIXON[2], M.D.

THERE has been a great deal of activity in public health in Philadelphia during the past few years. To mistake all activity for progress, however, would be a grave error. Sometimes in our American way of life we put value upon activity for activity's sake. On the other hand, for one who has been as closely identified with the situation as myself, it would be somewhat pretentious, if indeed not impossible, to identify true progress. I shall try to recount some of the major public health activities of the past few years and to recite some of the goals for the future.

The Department of Public Health in Philadelphia has three major parts: Philadelphia General Hospital, the Medical Examiner, and the old Bureau of Health, which has recently been renamed Public Health Services. All of these operations have significant public health implication, but I am sure that Arthur Parker Hitchens, whom we honor here tonight, would be most interested in the Public Health Services.

To understand what has been going on in public health, it is necessary to review a series of events involving all Philadelphia's government. In 1951, Philadelphia adopted a new city charter which set the stage for a tremendous change in city government. Dynamic leadership soon established new administrative standards for the city. There was a new personnel system based securely upon merit, and the development of sound financial policy including a program of planned capital improvement. And, above all, there was an ambition to make the services of government efficiently useful to the citizens.

Fortunately, also to set against this grid of public activity, there was a splendid study—the Philadelphia Public Health Survey of 1949—to guide the development of the program in this new situation. The activities of the past five years have, in general, closely followed this study. They may be conveniently grouped into the following classes: reorganization, development of a health code, program development.

It is common to say that "public health is people." In 1952, the public health services of the city might well have been characterized as resting in a series of pigeonholes, all of which were in the same desk but with very little communication between each other and with no common binding program force other than a nonspecific concern for the health of the people. The programs in each of these pigeonholes varied in competence, but there was one important characteristic—there were very few public health generalists, and it was rather like a community being served entirely by specialists with no general physicians.

Public health, like all other human group effort, requires organization. It was decided that these pigeonholes, some 23 in number, should be brought together into major divisions according to professional disciplines. So there were created four major professional divisions: preventive medicine, public health nursing, environmental sanitation and air pollution control, and mental health. These were supported by a division of health center administration, and staff offices of health education and research and statistics. Thus, all physicians other than psychiatrists found a common organization in one unit, all nurses in another, engineers and sanitarians in another, and psychiatric personnel in yet a fourth.

One of the immediate major problems was to generalize personnel. Previously, for in-

[1] Arthur Parker Hitchens Lecture IIc, College of Physicians of Philadelphia, 5 March 1957.

[2] Commissioner of Health, Philadelphia, Pennsylvania.

stance, there had been public health nurses for tuberculosis, for venereal disease control, for child health. The modern conception of public health nursing calls for a broadly-trained nurse who can function effectively in all these fields and many more. Through a superb job of in-service training, assignment and recruitment, there is now a generalized staff of public health nurses. The only problem, of course, is that we, like everyone else, never have enough. In a similar fashion there was developed a generalized staff in environmental sanitation and, more recently, in preventive medicine. Mental health was a new function in Philadelphia public health. This division was first established in 1954 and has been growing steadily since.

Through this reorganization of public health, general practitioners were developed to supplement specialized skills.

It became apparent that all public health could not be run from City Hall Annex. This was no new thought to Philadelphia, which had been a pioneer in the conception of community health centers. There was, indeed, already under way a plan for ten health districts. But the programs in these districts were uneasily related to each other through the Division of Health Center Administration. It was, at first, thought that each of these districts should act as a county health department, regarding the total department in the same light as a State health agency. But matters of uniformity of enforcement, program planning, and availability of personnel forced a reconsideration of this idea. Two arduous years were spent under the leadership of Dr. Ingraham in which the staff worked through to a satisfactory pattern of decentralization of program into health districts. Meanwhile a new program was evolved for the construction of district health centers. Previously these centers had been acquired by remodeling dwellings and other buildings, not necessarily well suited either in location or structure to health functions. The first two centers, new from the ground up, will be opened in 1957. Ground should be broken this year for two more; one of which will be the principal down-town headquarters of the public health services. It will house a new public health laboratory and will be closely related to the program of the Fife-Hamill Memorial Health Center. These new projects of bricks and mortar we expect to be useful for many years, but the organization of the people for public health services continues to change. Just recently, for instance, we have decided to create a fifth professional division of public health dentistry to recognize the increasing importance of dental public health and to foster its development.

I would not wish to leave the impression that merely because there has been change in organization we yet have all the personnel needed. It will only be on April 1 of this year that the first permanent director of Public Health Services reports for duty. Other important posts remain to be filled. We were fortunate, indeed, in being able to start with many fine staff, the majority of whom have stayed with the program through the exacting days of reorganization. Many fine new members have joined the staff in the past five years, and apparently word has gotten about the country that there is a true health renaissance in Philadelphia, for people are now beginning to want to come and work in this program.

One of the basic tools of public health workers is the health code. While public health is pulling sharply away from the extensive use of law enforcement as a program tool, nonetheless the basic responsibility of setting down the standards necessary for community protection in the law cannot be ignored. The Home Rule Charter called upon the Board of Health to recommend a new health code to the City Council. Such a code was signed into law on September 27, 1954. Nearly two years of work went into the development of this document which condenses into less than 40 pages the standards which shall be the basis of regulations adopted by the Board of Health. The procedure by which this code was developed deserves some comment. Countless hours of research, conference, and hearings were involved as the Department of Public

Health and the public health committee of the City Council worked together on its preparation. So well was the work done that the code was unanimously adopted by the City Council. The department is now working steadily in the development of regulations to implement this code. Here, again, it is using a democratic process of asking industry and community representatives to work together to produce useful, proper, and enforceable regulations. To date, of all the regulations adopted by the Board of Health under the code, only one set has been contested at public hearing.

In addition to the general health code, a special code, the Air Pollution Control Ordinance, was signed into law on March 9, 1954. This ordinance was the work of the Air Pollution Control Board, a special departmental board charged with the extraordinarily difficult tast of maintaining clean air for Philadelphia citizens.

So far we have acknowledged that public health personnel have a new organization, new bricks and mortar, and new laws. But, of course, this does not automatically improve the public health. This organization has been developing a good deal of public health program in the past five years. Most of this program is not new in itself, but constituted an extension of services already commenced and known to be necessary to the basic protection of community health. A description of a few of these programs may give some idea of what has been going on.

Fluoridation of a community water supply constitutes one of the most perfect examples of the mass application of preventive medicine that we know of. In 1954, Philadelphia commenced fluoridation. By that time, however, it had also moved forward upon a program to maintain the oral hygiene of all youngsters. This program is building up steadily each year in fine cooperation with the city's public and parochial schools, so that by 1960, when the effect of fluoridation is maximum, the service program will be at a level to effectively complement it. Dental caries, it must be remembered, is the most common illness of mankind the world over.

From teeth to mental health is a long jump. Since 1954, the development of mental health programs has been more rapid than any other public health effort. Not long after this new division was established it became clear that there was a large need for improvement of services to the mentally ill in Philadelphia. The wards of Philadelphia General Hospital were overcrowded and understaffed. Mentally ill were being sent to prison because there was no other place to go. It was estimated that some 20 additional clinics for services to children were needed. Unless these pressures for direct services could be met, it seemed unlikely that there would be much community sanction for the development of programs primarily for the prevention of mental illness, if, indeed, such programs can be truly developed on a public health basis. Fortunately, there has been a tremendous increased concern on the part of the Commonwealth to improve mental health services. Because of this interest, it has been possible to establish a reception center for the mentally ill, an expanded program of mental hospital extension services, and increased support to many community agencies. As a result, the mentally ill are no longer sent to prison, and while there still exists a serious shortage of facilities for long-term care, at least through the reception center the best possible use can be made of those facilities which are available.

It was early discovered that there were a great many persons who needed the help of a case worker, or psychiatrist, for themselves or a member of the household, who could not be served through the reception center. This information and referral service was commenced with a modest goal of 1,400 annual case load in 1956. It reached a case load of 2,000 in that year, and the load is still going up. Organizationally, both the State and the local programs are coordinated under the direction of the Director of the Division of Mental Health of our public health services.

Sanitation of the atmosphere is a matter of increasing concern to urban dwellers. The smoke nuisance of the past is well on the way to being defeated, although we still have burning dumps in Philadelphia. But there is now the new concern for smog and the uncertainty about the harmful and biological effects of end products of hydrocarbon combustion. New program for the control of air pollution has been developing patiently but steadily. Gradually there has been the introduction of laboratory techniques, of measurement, the enforcement of the air pollution code has been steppedup, and programing has been shifted from an emphasis upon answering complaints to a consideration of the special problems of regions and industries.

Like air pollution control, another program which has its organizational center in environmental sanitation is home accident prevention. Programing in this area is not as easy as it would first seem, but one part of such a program—that of helping to prevent or ameliorate the effect of accidental poisoning—has gotten underway. Interestingly enough, this poison information center is serviced by the Medical Examiner'soffice. This reflectsthe public health strengths which come from a federation of public health with other health services.

Another federation of importance has to do with efforts to reduce neonatal mortality. Here improved and devoted services at Philadelphia General Hospital have increased the infant salvage of babies born there. It has been observed here, as elsewhere, that mothers who receive inadequate prenatal care have abnormally high incidence of premature babies. Whether there is a causal relationship here is open to debate, but a prenatal clinic has been started in a health district to see if this will encourage more mothers to use prenatal services and to study the effect of such increased care on neonatal mortality.

These are just a few program highlights. There are still large gaps to be filled in what we would call "conventional" public health program. There is yet no overall programing in occupational health. Tuberculosis control needs to be adapted to fit changing conditions, and more attention needs to be paid to chronic illness. There are other programs in the developmental stage. It has long been suggested that Philadelphia seek a way to federate the work of the public health nurses in the official and voluntary agencies. Several years of community study and review may well lead, in the not too distant future, to the establishment of a new organization for extra institutional nursing services to people. Operating as an integral part of the decentralized health program, such a unit would greatly extend the possible use of nursing services. Not only are federated nursing services necessary to meet the public health needs, but also there is an increasing health problem as the cost of institutionalized medical care rises to make possible medical care in the home. We are in an aging population and older people need special services. One such service for older people, who also have mild problems of mental illness, is a plan now being jointly worked out by the Department of Public Health and the Department of Recreation. This calls for a special day-care program mildly therapeutically orientated. Such a service would encourage the keeping of older persons in their own households and would delay, if not minimize, the need for the use of institutions. According to the recent Kipps Bay Yorkville study, older people need above all, recourse to an information and counselling service. Not only in meeting their problems of health but also in other problems, such as housing and employment. I am inclined to think that this need is not limited just to the older folks, and that one of the principal public health contributions which could be made at minimum cost would be the establishment of a generalized health information counselling and referral service as a part of the district health program. It is difficult enough for the professional worker to find his way through the maze of interrelated community health

services. It must be nearly impossible for many citizens to do so.

Recently the Mayor of Philadelphia has adopted a community report establishing public policy in the field of the provision of medical care services to needy persons. A plan is developing to use the entire resources of the community—public and private—to meet this problem. New responsibilities may be thrust upon the health centers, not as outpatient departments, but as points of coordination of services to meet the medical care needs of needy people. Inevitably, medical care becomes one of the elements of personal health services about which public health workers, at least in urban communities, must be concerned.

From fluoridation to medical care, this has been a fragmentary account of public health activity in Philadelphia during the last five years. I have said something of its human resources, its program for the present, and its hopes for the future. With the help of the entire community, its government, voluntary agencies, physicians and its nurses, it would appear that Philadelphia is swinging into step with modern public health practice. This is the progress of public health in Philadelphia.

The Changing Scene in Harley Street[1]

By R. SCOTT STEVENSON, M.D., F.R.C.S. Ed.[2]

I

UNLIKE many of my distinguished predecessors in this Lectureship, I am neither a professional historian nor a professional philosopher. What talent I possess is as an observer, a reporter. I have "played the sedulous ape" (as my immortal namesake and fellow-citizen put it), not to Sir Thomas Browne but to Ring Lardner, and as models of literary style I most admire today those incisive essays that are published in *The New Yorker*—when I am able to disentangle them from the dazzling and mouth-watering advertisements among which they are hidden. My own English master at school was a follower of Walter Pater, and indeed it took me years of making notes of lectures at medical school before I finally rid myself of his elaborate arabesques. I have, of course, written a few books—but we are all authors and painters nowadays: there are one and a-half million amateur painters in England alone, *The Times* calculated the other day.

This is by way of introduction and excuse, and although my lecture tonight is in fact historical, as it should be according to the endowment, the heart of the matter—to which I will come in due course—will be to give you a brief, factual and objective account of what the National Health Service has done to Harley Street, that is to say, to consulting and hospital practice in London. And this may prove to be not quite what you expect.

II

As Lord Horder once said, an address in Harley Street is not really a higher medical qualification, and it is curious how this medical enclave developed—Harley Street, Wimpole Street and a few neighbouring streets. The development is quite recent: when I came to London in 1920 there were 330 doctors in Harley Street—in 1900 there had been only 157. By 1950 the number in Harley Street was 798, with another 580 in the neighbouring streets, or 1378 altogether. Last year, 1956, there were 796 doctors practising in Harley Street, but there was a total of 1450 when one included Wimpole Street, Devonshire Place, Welbeck Street, Queen Anne Street and Portland Place. So that private practice among consultants appears to be going up, not down.

I therefore wrote to the manager of the leading firm of consulting-room letting agents in the district, an old friend, and this is his reply: "The demand for consulting-rooms in the Harley Street area is greater than the supply, both for full-time rooms and part-timers. A part-timer usually only wants a room for one half-day a week—if he wants two or more half-days it is usually more advantageous to take a full-time room, as the rent is nearly as high. One reason for the demand being greater than the supply is that many of the houses in the first section of Harley Street (and also in adjoining streets) have been taken by solicitors, consulting engineers, surveyors and other non-medical people (including Actors' Equity)—there are only three houses in medical occupation on the east side of the first block in Harley Street, up to Queen Anne Street. Another reason is that an increasing number of the doctors practising part-time in Harley Street are not strictly consultants at all, i.e., they are not on the staff of a hospital."

Cavendish Square was laid out in 1720, when the great ground landlords of the West End of London began to encourage speculative building on their estates, and Harley Street was an insignificant side street leading north

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from the square. "The man in Cavendish Square" was Reynolds' epithet of scorn for the fashionable Romney. The first houses to be built and occupied in Harley Street were in 1752, and the first doctor to attempt to take up residence there was Robert Perrean in 1775. But to pay for his house he raised a loan from a banker by a forged bond and he and his brother were convicted of forgery and (as was customary then) publicly hanged.

The first physician of repute to live in Harley Street was Dr. James Latham, about 1800, who was on the honorary staff of St. Bartholomew's Hospital. It was not until 1860 that there were more than a score of doctors in Harley Street. Before then, the physicians and surgeons lived near their hospitals: some in "the City" close to St. Bartholomew's and the London Hospital, some across the river in "the Borough", near Guy's Hospital and St. Thomas's, another group around St. George's Hospital at distant Hyde Park Corner. As London grew and the West End filled up with houses, the doctors moved nearer their patients, first to Hanover Square and the neighbouring Savile Row, and then across Oxford Street to Cavendish Square and slowly up into Harley Street. An important reason was its proximity to the chief railway stations, for the leading physicians made much of their incomes from train journeys into the Provinces two or three times a week, at a guinea a mile.

In Victorian and Edwardian days the consulting physicians and surgeons were centred on London and were wealthy men who lived well, usually with private means, and found the substantial houses of Harley Street to suit their habit of frequent and lavish entertainment, for doctors who sent them patients expected in those days to be asked to dinner and meet the fashionable world. They all had butlers, coachmen and several servants, and their carriages and horses were stabled in the mews behind their houses. Some surgeons became famous for their dinner-parties, such as Sir Henry Thompson with his much sought-after "octaves"—eight guests, eight courses, eight wines, and Sir John Bland-Sutton, with his breath-taking Assyrian hall and beautiful Assyrian silver.

It was most unusual for more than one physician to practise in a house, and when two nameplates appeared they would be of father and son or of two brothers. Today some houses have twenty nameplates. I remember as a boy driving for the first time down Harley Street in a hansom cab with my father in the summer of the year 1902, and I was struck especially with the wonderful display of the flowers in the window-boxes of every house in it. In those days the physicians all wore whiskers, tall hats and frock coats, they wrote their letters with their own hands after dinner, and few if any had a private telephone. Electricity did not begin to displace gaslight in Harley Street until the year 1909, and horse carriages were at least as common as automobiles until the outbreak of war in 1914—indeed, the Army Transport in France in that year was all horse-drawn. The year 1914 marks the end of the golden age of medicine in Harley Street—it was War not Socialism that finished it.

One of the few who maintained the old fashion of Harley Street entertaining after the first World War was my friend Dr. George Cathcart. He was a bachelor, son of a wealthy Edinburgh wine-merchant (who sold claret, unlike Ruskin's father, who sold sherry), and when I think of him I can see him, in his heyday, sitting with a benevolent smile in his black velvet tuxedo at the head of the long table in his panelled dining-room. At either end of the room were cabinets lit up by electricity, containing his collection of eighteenth-century glass, massive pieces of old Irish cut glass stood on the Sheraton sideboard, eight or ten candles in old glass candlesticks illuminating the table. Around his hospitable board one was accustomed to see singers from the Covent Garden opera, Sir Henry Wood the conductor and other musicians, Edmund Gwenn and other actors of the more serious

kind, patrons of music and the arts, diplomats, politicians, and plutocrats from the City, and the leading family doctors in the West End of London, for in those days most of them were Scotsmen.

George Cathcart loved old waiters and disliked taxi-drivers. I have known him, after grossly over-tipping the waiter at the Café Royal or Romano's ("Always leave a glass of wine in the bottle for the waiter", he used to say), to drive home in his astrakhan-collared coat and hand the taxi-driver threepence (five cents) over his legal fare, while I hastily ran to open his front door to avoid recriminations. We gave him a sherry party at the Royal Society of Medicine to celebrate his ninetieth birthday, and Miss Anna Neagle, our leading English film star (upon whom he had operated without fee when she was a little chorus girl) gave up her holiday in Italy to come back and cut his birthday cake. He died happily, having spent all of his fortune, at the age of 92.

The last private non-medical resident in Harley Street was Sir Kynaston Studd, who was a wealthy City merchant and had been Lord Mayor of London; he lived at 67 Harley Street until he died in January, 1944. Today there are no houses in Harley Street in one private occupation. Many have consulting-rooms on the ground floor and first floor (second floor, you would call it) and apartments above, some have been converted into residential apartments. We, too, have traffic problems in London, and Harley Street is now a one-way thoroughfare, with traffic-lights at every intersecting street. No longer does one see a troop of jingling Horse Guards clip-clop down Harley Street in the middle of the morning, oblivious of the traffic, on their way from Regents Park barracks to mount guard in Whitehall, as they used to do when I lived there before the last War. And Sir Arbuthnot Lane once told me that he used to drive from Cavendish Square across London to Guy's Hospital more quickly in his carriage and pair before 1914 than he did in his Daimler automobile afterwards, because of the enormous increase in traffic.

III

In my younger days it was unusual for a doctor to contemplate practising as a consultant in London unless he possessed private means, for the junior appointments in hospital were unpaid and the early years in consulting practice were inevitably far from remunerative. Soon after I came to London in 1920 my good friend Dr. George Cathcart took me to dinner with Hunter Tod, then the leading otologist in London, a "brither Scot", the son of a Glasgow ship-owner. Dr. Cathcart said that I was contemplating starting practice in Harley Street, and Hunter Tod said to me: "No man can practise as a specialist in London unless he has a private income of at least £2,000* a year". I replied: "I don't want to appear discourteous, but don't you mean that *you* have £2,000 a year and cannot contemplate anyone managing on less?" Dr. Cathcart chimed in that he had begun practice in Harley Street in 1892 with £400 a year of his own, besides what he earned as a private assistant and from his practice, and that, in the words of Dr. Samuel Johnson, was "wealth beyond the dreams of avarice".

Lord Horder once told me that he was the first consulting physician appointed to the honorary staff of St. Bartholomew's Hospital who had not a private income. He was, in fact, asked by the Board of Governors how he intended to support himself, and he answered, "By the practice of medicine"—and did. Many consulting physicians and surgeons taught physiology or anatomy in the medical schools attached to the hospitals in London, for modest salaries, which, however, kept them going until consulting practice came along. For example, Sir Alfred Fripp (according to his biographer, Cecil Roberts) when he

* I hope I may be forgiven if throughout I write "pounds" and not "dollars". To translate at the current rate of exchange gives little idea of the true value of the pound at that time—or indeed today.

began had £180 from his father and £360 a year as a demonstrator of anatomy at Guy's Hospital.

Many doctors used to prepare for consulting practice by a few years in general family practice—my old chief, Irwin Moore, was for five years in general practice at the hunting centre, Market Harborough, Sir James Dundas-Grant was in general practice in the East End of London, while the leading laryngologist of my day, Sir St. Clair Thomson, was for several years in general practice in Florence, Italy, before coming to London.

After a year or two in general practice Conan Doyle, who was a graduate of Edinburgh, resolved to practise as an opthalmic specialist in London. He was advised to spend six months in Vienna, and he himself said that he spent four months there; but his indefatigable biographer, Hesketh Pearson, searched his diaries and found that he actually spent only two months in Vienna, before he began practice on 6th April 1891, at 2 Devonshire Place, London (a continuation of Wimpole Street), in a consulting-room that cost him £120 per annum. I wrote recently to the secretary of Moorfields Hospital (then, as now, the chief centre of postgraduate instruction in ophthalmology in London) about Conan Doyle, to know whether he had had any training there, but the secretary replied that there was no record of his having been a pupil or clinical assistant. Perhaps fortunately for everyone concerned, he did not see a single patient and spent his time writing the first Sherlock Holmes stories, which were at once accepted for publication and eventually made his fortune.

Nowadays, for good or ill, there is a gulf between general family practice and consulting (hospital) practice, and I cannot see ever again a general practitioner practising a specialty part-time, working in a hospital and taking a higher qualification, and eventually deserting general practice for a specialty—as, indeed, I did myself. Whether this is a good thing or a bad thing remains to be seen, but it is true that the National Health Service in England has divided the medical profession permanently into general practitioners, consultants (on the staffs of hospitals), and public health officers. The number of consultants and specialists outside London has greatly increased, the general standard in the country is undoubtedly higher, and the "part-time specialist" has gone.

IV

The National Health Service Act, which came into force on 5th July, 1948, was the culmination of a long series of attempts to improve the general health and well-being of the population. In England, modern health legislation dates from the Health Acts of 1848 and 1875 in the reign of Queen Victoria, and much progress was made in the amelioration of social conditions during the last two decades of the nineteenth century. The Report of the Royal Commission on the Poor Law in 1909 showed that the medical care of the population was inadequate and that much poverty was due to ill-health. Mr. Lloyd George visited Germany in 1907, to study the German system of State sickness insurance, which had been invented by Bismarck in 1883, primarily as a bulwark against Socialism; he came home much impressed by the success of the German system, and introduced his National Insurance Bill in 1911, intending to carry out the administration of the scheme through the Friendly Societies and to place the doctors under their control; but the doctors put up such a determined opposition to this that special "Insurance Committees" were formed to deal with the administration, upon which the doctors were represented. This Insurance Scheme, paid for by equal weekly contributions from workers and employers and from the State, covered only workers under a certain annual income but not workmen's wives and children, so that more than half the population in the lower income groups were not insured. The doctors were paid part-time quarterly salaries, based on capitation fees. An important deficiency, however, was that consultant, specialist, and hospital services

were not included—in other words, if a worker caught a cold he was looked after by an insurance doctor, but if he got appendicitis he had to go into hospital and be cared for by charity, operated on by an "honorary" surgeon. Nevertheless, with all its defects, the National Insurance Scheme worked, and very few changes were made in it between 1912 and 1939. During the years of depression and prolonged unemployment, in the industrial districts of South Wales and the North the doctor was the only man who ate three square meals a day.

The outbreak of war in 1939 was the most important influence in integrating the working of the voluntary (charitable) hospitals and the local authority or municipal hospitals; some of the voluntary hospitals were medieval foundations, many were charities founded in the eighteenth century, while the local authority hospitals were grim institutions set up by Dickensian "Boards of Guardians" for the reception of the indigent chronic sick, though later they also accepted acute cases. These former Poor Law hospitals had been placed under county councils and county borough councils by the Local Government Act of 1929, and some of the wealthier county councils, such as Middlesex and London, developed municipal hospital services that, with staffs of visiting consultants, were as efficient as the best voluntary hospitals. At the time of the Munich crisis in 1938 the Ministry of Health made a survey of hospital accommodation throughout England, and an Emergency Medical Service was organised by the Ministry to deal with the expected air-raid casualties, 290,000 beds being provided chiefly in municipal hospitals, fever hospitals and mental hospitals on the outskirts of or well outside the chief cities of the country, the staffs being taken from the honorary and resident staffs of the voluntary hospitals. The hospital part of the National Health Service was built upon the foundations of this wartime Emergency Medical Service. I remember going at this time to see a friend who was a senior official at the Ministry of Health on business connected with my hospital, and he said to me: "The Ministry has its thumb on the neck of every hospital in England, and it is never going to take it off." I didn't believe him—but it was true.

In December, 1942, at a critical period of the second World War, when the bombed people of England were feeling closer together than ever before—or since, the famous Beveridge Report was published and received with universal enthusiasm, for it seemed to show that it could indeed be possible to abolish poverty and unemployment, one of the main assumptions being a comprehensive health service available free to all members of the community. Under Mr. Churchill's Coalition Government, in 1944, a scheme for a National Health Service was put forward for discussion, the proposals including that the scheme should be universal, available to rich and poor alike, that it should include specialist and hospital services as well as those of the family doctor, that it should be free of charge, the cost being borne by rates and taxes and a special social service contribution, and that the development of health centres should be encouraged. The Service was to be managed by grouped county councils and the voluntary hospitals were to continue as such.

When the Labour Government came into power after the General Election of 1945 Mr. Aneurin Bevan became Minister of Health and made some important alterations and additions to these proposals, mainly by bringing all the hospitals—voluntary and local authority alike—under the ownership of the State, and by abolishing the old-established custom of buying and selling the practices of family doctors, the doctors being adequately compensated for this innovation. Mr. Bevan's discussions with the doctors were sometimes acrimonious but in the end the agreement arrived at was a comparatively friendly one. The voters were determined to have the Health Service universal, without an income limit, because the "means test" for public relief during the periods of unemployment between the Great Wars had been heartily detested by

the workers and their families—and the representatives of the workers were now in political power. They were also determined that the voluntary hospitals should no longer be charitable institutions—the lovely word "charity" has become a dirty word in our country, and the ugly words "national assistance" have taken its honorable place.

Mr. Aneurin Bevan once said to me, wagging his finger for emphasis: "My duty as a Cabinet Minister was *to establish the right* of every man, woman and child in this country to a health service free at the time it was needed. It is up to the doctors to make it work". My own view is that, much as I dislike his politics, Mr. Bevan was a far-sighted Health Minister: he decided to base the principle of medical staffing of the nationalized hospitals upon the traditional voluntary hospital consultant method and not upon that of the local authority institution—and this in face of the opposition of many of his own Socialist Party, who had made their political reputations in the local politics of town and county councils and were proud of the improvements they had achieved in the old Poor Law hospitals. We might well in England have had a utilitarian hospital service like the old workhouse infirmary type, with full-time medical officers (a policy to which the Socialists were committed) under the yoke of a lay committee, lower standards, more bureaucratic, and a feeling of helplessness and frustration among the doctors. Mr. Bevan, having already made a reputation as an orator, was anxious to make his reputation as an administrator. He was determined to build up his Health Service on a unified hospital system by satisfying the medical staffs of the leading hospitals. He achieved this successfully by negotiating with the Presidents of the Royal Colleges of Physicians and of Surgeons behind the back of the British Medical Association, by surrendering everything they asked for, allowing part-time private practice (only 1600 out of over 5600 specialists are full-time), and especially by giving the 36 "teaching hospitals" in the country separate Boards of Governors and almost complete independence, and letting them keep their old endowments.

One of the methods by which the leading consulting physicians and surgeons were persuaded into the Health Service was by the institution of what are called "merit awards", an idea for which Lord Moran, late President of the Royal College of Physicians, claims the credit. A semi-anonymous committee of retired consultants is appointed by the Minister of Health, after consultation with the Royal Colleges, with Lord Moran as its salaried chairman, and this committee confers "awards" on selected consultants "in recognition of special contributions to medicine, exceptional ability, or outstanding professional work". Four per cent of all consultants are eligible for the first grade of £2500 per annum additional to their ordinary (usually part-time) salary, ten per cent are awarded the second grade of £1500 per annum, and twenty per cent the third grade of £500 per annum. These annual awards go on as long as the consultants are in the Service, and their names are not published. There has been nothing like it in England since the days of Sir Robert Walpole in the eighteenth century.

Unfortunately the National Health Service has proved much more expensive than was expected—the first estimate by Mr. Bevan was that it should cost £152,000,000 per annum, but last year, 1956, it reached £475, 000,000. In consequence capital expenditure on much-needed new hospital buildings, health centres, and even on repairs has had to be kept down to an absolute minimum. One of the chief difficulties has been the drug bill, which has reached around £50,000,000 per annum. Can our country afford it?—well, last year it could afford £840,000,000 for tobacco, so one presumes that it can.

There are 2,688 hospitals in England and Wales, 996 of them former "voluntary" hospitals and 1,545 former "local authority" hospitals; a small number of hospitals were exempted from the Health Service at the time

of the take-over in 1948, mainly hospitals run by religious bodies or small private sanatoria, but including also the well-known Royal Masonic Hospital and the Trades Unions' own Manor House Hospital. As I have already observed, the "teaching hospitals" associated with medical schools are in a privileged position, each with its own autonomous Board of Governors and its endowments intact; the other hospitals are less fortunate, their endowments having all been sequestrated, and they are administered by 14 Regional Hospital Boards appointed by the Minister, each region having a population of about 3,000,000. The individual hospitals are more intimately managed, usually in small groups, by Hospital Management Committees, of which there are 377, appointed by the Regional Board. Medical staff committees do exist, but they have no statutory place in the scheme; they are only advisory and often completely disregarded.

The medical schools of the teaching hospitals of London are not under the National Health Service; like our universities, they are financed through the University Grants Committee (a method of distributing State money which, like the Medical Research Council, could be copied elsewhere with advantage); nominally under the Privy Council, this committee has a completely free hand in the distribution of over £30,000,000 per annum. In addition, last year, 2½ million pounds sterling were spent on medical research—and over 60 million pounds on atomic research.

The teaching hospitals have been given a special status which affords them plenty of scope. But this separation has to some extent harmed the training given in some of them, because they tend to be cut off from the everyday work of medicine done in the regional hospitals, and are liable to become collections of special departments doing specialist work at a high level. Instead of getting a broad view of medicine or surgery by apprenticeship to a general physician or surgeon as in the old days, the student may "clerk" or "dress" for someone interested only in leukaemia or arterial grafting; and the apprenticeship system will therefore have to be supplemented more deliberately by tutorial or other methods designed to put the specialties in perspective. In my own specialty, Dr. Simson Hall of Edinburgh, the leading teacher of otolaryngology in Scotland, told me only the other day that he now never performs a tonsillectomy or a nasal septum resection before students in hospital, his two operating sessions per week being fully occupied by doing one or two fenestrations, stapes mobilizations or tympanoplasties under the operating microscope. Today the obligation of the surgical instructor to medical students is mainly to teach the elements of surgical diagnosis and the possibilities and scope of surgical treatment; technical aspects of surgery have become—rightly—entirely a postgraduate study, and our medical curriculum urgently requires revision to give proper effect to this.

VI

Since the institution of the National Health Service, the postgraduate training of the prospective consultant has become much more systematic and thorough; and as all his appointments are paid his former financial worries (partly solved by coaching, doing evening "surgeries", teaching, journalism) have largely disappeared.

After five years as a medical student the young graduate must now do one pre-registration year as an interne, six months medicine and six months surgery. Then he is usually called up for his two years National Service; he may be deferred for another six months or—rarely—even more, depending on the Service requirements at that time. Calling up is controlled by the Central Recruitment Committee of 45 members, representing the Royal Colleges and other medical organisations, predominantly the British Medical Association, which nominates 27 members of the 45. Representatives of the Services and of other Government departments (Health,

Labour, Medical Research Council) attend as observers. It delegates executive authority to a Service Sub-committee of 23 members, the secretary of which is a B.M.A. assistant secretary.

If the young man's aim is to become a consultant surgeon he must get his Primary Fellowship of the Royal College of Surgeons—if he is lucky, while still in a Service, or he may get a demonstratorship of anatomy when he leaves his Service, or he may do the three months special course at the Nuffield College of the Royal College of Surgeons. Last year (1956) only 174 candidates out of 830 (all of them well prepared) were successful in the Primary Fellowship; and in addition only 191 candidates out of 722 were successful in the Final F.R.C.S., so that one need hardly be surprised that the young surgeon wishes to emphasize his Fellowship by calling himself "Mister" instead of "Doctor". Some of these candidates may, however, have sat at more than one of the examinations—three Primaries and two Finals take place each year. These figures have been supplied to me by the Royal College of Surgeons, but I may say that the Royal College of Physicians courteously but firmly stated that their figures are not published: I gather, however, that less than 10 per cent of the candidates for its Membership—the M.R.C.P.—are successful; there is no examination for Fellows, who are elected (sometimes with much heartburning) from among the Members.

The young prospective surgeon or physician then gets a post, still resident, as Senior House Officer, which he holds for a year, treating emergencies and probably other cases on his own responsibility. Then he is appointed Registrar for two years and is expected to get his final F.R.C.S. or M.R.C.P. during this time. He cannot become a Senior Registrar without the F.R.C.S. or similar higher qualification in his specialty (M.R.C.P. or M.R.C.O.G.—Member of the Royal College of Obstetricians and Gynaecologists), and he holds that office for four years, when he becomes eligible for a consultant's post. While a Senior Registrar he will be well advised to take a university higher degree, the M.D. or M.S., and publish some original work. He will also be well advised to make himself *persona grata* with his chief—for without influential backing he will never achieve an appointment as a consultant, so keen is the competition. In all of these appointments he is adequately, though not lavishly, paid.

He is now aged 32 or 33, and will appear before committees, be put on short lists, and spend agonizing months with his Registrarship behind him and the mirage of a consultant appointment in front of him. He begins to feel that life is too short—and that perhaps he was rash to marry and have a couple of children on his prospects.

In a report from the South-East Metropolitan Region (*B.M.J.*, Oct. 20, 1956, Supp.) it was stated that in the years 1952–56, 67 Registrars in that area completed their training and 22 became consultants (17 more, to my surprise, became Senior Hospital Medical Officers, a grade I had thought was being abolished, i.e. doing consultants' work but without their status or salary, usually because of not possessing a higher qualification); 9 got another Senior Registrar appointment, and 19 were lost to the hospital service. A leading surgeon writes to me: "My own feeling is that we are producing too many specialists at too high a rate, and therefore there is a surplus."

VII

There is no doubt whatever, whether one likes the idea or not, that the National Health Service, so far as consultant and hospital practice is concerned, has become acceptable to the doctors in Britain. It is true that at this moment a violent controversy is going on between the doctors and the Government—be it noted, a Conservative, not a Socialist, Government—but that is with the general practitioners or family doctors, because of the disputed financial agreement (the Spens Report) on which they had been persuaded to

enter the Health Service, based on the cost of living and the comparable incomes of other professions.

As regards consultant practice, Mr. Holmes Sellors, chairman of the Central Consultants and Specialists Committee of the British Medical Association, said on 28th November, 1956: "A State medical service had come to stay. On the credit side, it had probably led to improvement in the general standard of hospital practice, particularly in the periphery. Consultants and specialists had greater security and superannuation rights." The Fellowship for Freedom of Medicine, which was founded by Lord Horder in 1948, advertises that it "aims to free medicine from the influence of party politics, to maintain the highest standards of medical practice, and to see that the individual general practitioner and consultant can practice the art and science of medicine unhampered by State interference." Yet at its annual general meeting on 10th November, 1956, Mr. Dickson Wright, who had been one of the most eloquent opponents of a National Health Service, began a speech as follows: "While appreciating that a National Health Service is necessary . . ." In deference to protests from the meeting he modified this to: "While appreciating that a Health Service is desirable . . .", and in this form the resolution was carried.

I wrote on this subject to a friend of mine in London, one of the most famous consultant surgeons in Britain, anti-Socialist and distinguished in the War, and here is his reply: "The hospitals have been saved by the State, and the physicians and surgeons are doing well in these bad economic times. The general practitioners have a settled income and the good ones have time for some private practice and time for any clinical research they want to do. The young consultants get a living wage straight away when they are appointed and do not have to wait for years until practice matures. There is no difference at the hospitals between the senior and junior consultants. I have nothing against the Health Service itself, I have against income tax and surtax, which collect most of what we earn. There is no doubt whatever that private practice is diminishing every year, for nearly everybody wants to come to hospital for treatment."

VIII

In England there has in recent years been a great increase in legal actions against doctors; but this is more likely because of what is called "legal aid" than of any feeling about the nationalization of the health services.

To get a certificate for legal aid the applicant has to qualify on two counts: (1) He must satisfy a committee of the Law Society (the official organisation of the solicitors) that he has a *prima facie* case; and (2) he must satisfy the National Assistance Board that his income and capital are below certain limits. The Board will then determine if he is entitled to a "*nil*" certificate, i.e., he will not be liable for any costs, or what amount he will have to contribute. The limits have not been raised since the scheme came into force some years ago, and most people, unless they are old age pensioners or on sickness benefit, have to contribute a substantial sum to their costs, which may, however, be paid by installments. This usually will be less of a deterrent in an action against a doctor or hospital, as the claimant will usually still be on the sick list.

On the validity of the case, the committee consider it in the first place on the written statements of the applicant and any witnesses he may have. If they are not satisfied that the facts as stated give rise to an action they refuse a certificate; the applicant can then appeal, and is given a hearing by the committee (and can, at his own expense, be represented then by a solicitor or barrister). The committee appears to deal very fairly with the matter and do not grant a certificate unless the applicant has a reasonable chance of success—but they have no means of testing the applicant's story and have no information at all about the other side's defence.

Some of the consequences of so many legal

actions are that many quite unnecessary X-ray films are taken, the young surgeon sometimes feels that a lawyer is looking over his shoulder as he operates, and hospital committees refuse to allow house officers (internes) to give anaesthetics or to do even minor routine operations except under the direct, personal supervision of a consultant.

IX

This, then, is the factual and objective picture I promised of what has been rather unkindly termed "socialized medicine". The system demands eternal vigilance on the part of the doctors, for the threat to their independence still exists. The scheme is not designed for export, and building it into its present form has been slow, gradual and sometimes patchwork. I do not advise other countries to follow in our footsteps, and personally I have always maintained that State-supported insurance and block grants for the care in the voluntary hospitals of State-insured patients would have been a simpler and less expensive method of dealing with this problem, even though hopital costs have gone up enormously—I know one hospital which cost £100,000 a year before the War and last year cost £1,600,000.

But ours is a truly democratic country, where the voter—the ordinary man and woman in the street—in the end controls policy, and all political parties were determined to have a National Health Service. Harley Street—consultant and hospital practice in England—is no longer what it was when I was young, but it continues to flourish in this changing world and has adapted itself successfully to the social ethic and collective spirit of today.

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I have to thank many kind friends for up-to-date information on the subject of this lecture, especially Mrs. Bryant of the Howard de Walden Estate Office, Mr. Owen of Messrs. Bedford & Co., the estate agents, the secretary of the Royal Ophthalmic Hospital (Moorfields), Dr. Angus Macrae, secretary, and Dr. Stephen Hadfield, assistant secretary, of the British Medical Association, Dr. E. C. Warner, F.R.C.P., Dr. T. F. Fox, editor of *The Lancet*, Mr. J. Chalmers Ballantyne, F.R.C.S., Dr. I. Simson Hall, F.R.C.S. Ed., Mrs. Grieves of Messrs. Amphlett, solicitors, and others who wish to remain anonymous.

John and William Hunter and Some Eighteenth Century Scientific Moods[1]

By JANE M. OPPENHEIMER[2], PH.D.

I AM especially happy to have the privilege of speaking to your Section on Medical History, because I am so deeply obligated to the College of Physicians for its repeated kindnesses, which have been a primary factor enabling me to carry out whatever work I have attempted on the Hunters. But there is more involved than the excellence of the collections and the helpfulness of the staff.

William Hunter, who already then had a strong interest in obstetrics, made a trip to Leyden in the spring of 1748 and visited Albinus. In July 1748 John Redman, your first President, was awarded the degree of Doctor of Medicine at Leyden, having worked with Albinus and having written his thesis on an obstetrical topic. I do not happen to know whether William Hunter and John Redman met in Leyden in 1748 or in London the next year when Redman was at Guy's, but it is at least a possibility. In any case, we do know that three of the twenty-four Founders of this College, John Morgan, William Shippen Jr. and Benjamin Rush were students of the Hunters. John and William Hunter are neither of them very far from us here.

It is in part because they had so many connections, as teachers and friends, with people of personal consequence to us that the Hunters continue to be a source of interest. We derive some of our ideas from them; we value them because of their ideas; and what I wish to do is raise a few questions about the type of ideas they had.

Much of what is known of them (1) contributes to the delineation of their differences of character. William seems to us highly polished and elegant, erudite and constrained. John, in contrast, looms up a less scholarly figure. He is rougher and blunter, expressing his frank and original opinions not only more freely but more crudely. His primary attribute seems an abundance of physical and intellectual energy, of warmth and vitality, that spills over into a flood of creative effort rarely paralleled in the history of biology and medicine. "My mind is like a bee-hive," he said to John Abernethy, and Abernethy, one of the most distinguished of his students and followers, adds, "The simile struck me, on account of its correctness. For, in the midst of buz [*sic*] and apparent confusion, there was great order; regularity of structure; and abundant food, collected with incessant industry, from the choicest stores of nature" (2).

A contrast between the Hunters becomes clear however not only from consideration of the anecdotes handed down about their lives (3), but also from examination of the quantity and variety of their published works.

We might begin with an evaluation of those of the elder brother (4). Three books by William Hunter have been published. The posthumous *Two introductory lectures* (5), while of great interest for the light it casts on William's character and on the quality of his teaching, is not especially relevant for our discussion here. His important book was the great folio *Anatomy of the human gravid uterus* (6). This was in course of careful preparation for over 30 years. In the styles of its writing, its illustration, its printing it was nothing short of magnificent, and the subject-matter was deserving of the format. I would wish

[1] Presented before the Section on Medical History of the College of Physicians of Philadelphia, 4 December 1956. This meeting celebrated the recent restoration of the Hunter homestead, at Long Calderwood, Scotland, as a memorial to John and William Hunter.

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some one in this audience closer than myself to William's profession to comment on present opinions as to the quality of its contents; but surely it remains one of the truly great anatomical monographs of history.

The first of his books to have been published during his lifetime, the *Medical commentaries* (7), did not purport to be unified in content and covered a number of separate subjects, many of them specifically related to his various scientific controversies which do not concern us here. The *Medical commentaries*, however, also included a small number of essays relating to his anatomical discoveries that might just as appropriately have been published in periodicals and which can be considered together with his articles of the latter type. His actual publications in periodicals numbered about 18. If we consider the subjects covered in these and in the relevant comparable essays in the *Medical commentaries*, we find that we can categorize them without too much difficulty. Seven of the essays or articles dealt with one or another aspect of the circulatory system (including the lymphatics), the same number with the skeleton (including one on tendons). Four related to the reproductive system, the subject of his big monograph. The rest dealt with a few miscellaneous other subjects: emphysema, the cellular membrane, the pupillary membrane; signs of murder; a disorder of the stomach; the lacrymal ducts; an autopsy report; a description of an animal from India. Clearly there is some breadth of range here, but it is a limited one.

The accomplishments of John were very different indeed. He published three books in his lifetime: *The Natural history of the human teeth*, *A Treatise on the venereal disease*, and *Observations on certain parts of the animal oeconomy* (8). The *Animal oeconomy*, like William's *Medical commentaries*, consisted of a group of separate short essays, some of which had been and the rest of which might have been, so far as their character was concerned, published in the *Philosophical Transactions of the Royal Society*. John's fourth book, *A Treatise on the blood, inflammation and gun-shot wounds*, virtually ready to go to press when he died, appeared the year after his death (9). Like William Hunter's monograph, this too was in preparation for over 30 years. It lacked the felicity of William's style, and its single-mindedness. But it was crammed full of observations and ideas, and had John written nothing else in his whole lifetime it would easily have made his fame.

John's short papers are extraordinarily difficult to count and to classify, even more so than William's. Some of his articles, like the 6 Croonian Lectures delivered at the Royal Society, were not published in his lifetime but were later included by Owen in his edition of the *Animal oeconomy* which forms volume 4 of the posthumous collected *Works*. Some articles were during John's lifetime and with his authorization written and prepared by his brother-in-law Everard Home; in these cases Home's name is published as author, but the titles specify that the materials were furnished by Hunter. John also published several anatomical notes in John White's *Journal of a voyage to New South Wales* and in Alexander Russell's *Natural history of Aleppo* (10), all of which might appropriately have found their way into periodicals under other circumstances. In any case, the number of short articles that can be ascribed to John (including those in the *Animal oeconomy* and in the books by White and Russell) is over 50, thus well over twice the number of William's short articles.

Comparison, however, of the number of published articles of the two brothers is limited in value by the fact that a great bulk of John's materials was still unpublished at his death. It is commonly believed that Sir Everard Home, one of his executors, who burned the majority of the manuscripts, based many of his own articles (11) on Hunter's manuscript materials; however some of the latter, copied by William Clift before the originals were burned, have been published either in the catalogues of the museum collections, or in the *Essays and observations on natural history*,

anatomy, physiology, psychology and geology which Richard Owen edited and published in 1861 (12).

It is not, however, through sheer force of quantity, but rather by virtue of the bewildering variety of topics covered, that the work of John differs from that of William. The subjects of William's interests, you will remember, fell into a small number of natural groupings. John's completely defy classification: even the published articles, which probably represent only a minority of his fields of investigation, cover topics as diverse for instance as postmortem digestion of the stomach (1772), airsacs in birds (1774), production of heat by animals and vegetables (1775), apparent transmission of smallpox from mother to fetus (1780), organs of hearing in fishes (1782), descent of the testis (1786), structure of the placenta (1786), secretion by the crop of the breeding pigeon (1786), olfactory nerves (1786), extirpation of one ovary (1787), comparative observations on wolf, jackal and dog (1787), structure and oeconomy of whales (1787), introsusception (1789), horny excrescences of the human body (1791), bees (1792), fossil bones presented to the Royal Society (1794), etcetera etcetera.

Small wonder that John's literary style fell below his brother's; he occupied his time with experiments and observations, accurate to a high degree, rather than in perfecting his prose. If William, however, concentrated on more circumscribed subjects than John (13) and approached them with a higher degree of perfectionism; and if John expended his energies on far more diversified aspects of natural history, morphology, physiology and pathology, in his efforts to place surgery on the broadest possible biological basis, yet still there were some features common to their modes and moods of work.

For instance we have been thinking of both of them, simply because it comes natural to do so, as scientists, though William was strictly a medical man, and John technically a surgical one. In both cases, their contributions went beyond those of sound practitioners and inspiring teachers, and popular and successful though they became in these phases of their callings, their great gifts were as investigators. They made scientific discoveries, and important ones. Even when the subjects of their writings were frankly medical or surgical in content, they were not mere case reports; their intent was always implicitly investigative in the broadest sense of the word.

Furthermore, whether they dealt with materials from their practise or from the field of natural history or whatever, they both exhibited in common the characteristic that as scientists they particularly excelled as investigators of the concrete. They observed; and they preserved; and what is perhaps most noteworthy in their writings is that they refrained completely from the construction of elaborate theories designed to encompass every observed fact in a single synthetic system.

This is perhaps the more remarkable in the case of John, who had a strong speculative cast to his mind, as is demonstrated, for only one instance (there are many more), by his development in the *Treatise on the blood, inflammation and gun-shot wounds* of the theme that the blood is alive. He thought often in terms of general principles: "In the works of Nature, where we see a similarity in principle, or effects produced from similar causes, it is reasonable to suppose that they [those works] are similar in their great principles, and therefore may arise from one cause" (14). But his especial talent was for the marshalling of facts, and as one of the Hunterian Orators has so well said, "His hypotheses . . . never diminished his zeal for facts" (15).

Anatomy in general in Great Britain at the time of the Hunters was a science based principally on observation, which is particularly noteworthy only because it stands in such sharp contrast to conditions elsewhere. In Germany in particular a strong movement was developing towards what is often called transcendental anatomy, which relied on the concept of Unity of Type. This held not only

that each organism (or organ) presents its own modifications of one ideal Type or Archetype, but also that the variations are significant only insofar as they are subservient to the Type. The anatomist who clings to this doctrine sees his primary task as inferring from the observable modifications what the theoretical Archetype might be. He thus becomes almost more a philosopher than a scientist; and on the Continent *Naturphilosophie* became the predominant, if not the exclusive, mood of many of the most influential minds (16).

Naturphilosophie prided itself on subjectivity, not objectivity, resting to a far greater proportion than science proper on intuitive rather than observational phenomena. Hence it has sometimes been called romantic philosophy, and the biology which it fostered was in a sense romantic biology, just as the history which grew out of it was romantic history, and the literature romantic literature. Now to what degree, and this is the primary question which I wish to leave uppermost in your minds, were the Hunters involved in the fact that when the romantic movement was to flourish in England, it became largely a literary movement and did not grow into a scientific one also, as abroad?

We have been speaking this evening of connections; and the specific connections between the Hunters and the romantic movement were not so remote as might seem on first thought. On the literary side, John and William's sister Dorothea was the mother not only of Matthew Baillie the pathologist, but also of Joanna Baillie, the distinguished poetess and dramatist who was for a half century the close friend of Sir Walter Scott (himself, by the way, the grandson of a distinguished Scottish physician). William Hunter seems to have been a friend of Allan Ramsay the younger, whose father, like the Hunters born in Lanarkshire, was one of the heralds of the literary romantic movement in England. Robert Burns was an admirer of poems written by Mrs. John Hunter; and in fact, some of her own poems ("My mother bids me bind my hair," and "The Spirit song," for instance) were themselves lyrics with a strong romantic undertone.

On the scientific side, John's significance for the fate of transcendental anatomy in England could hardly have been more direct, since the one English anatomist who was most influenced by *Naturphilosophie* and who spoke up most strongly for it was none other than Richard Owen, who, though his life failed to overlap in years that of John, yet derived his intellectual descent almost immediately from him.

Owen's first position in London, as a youth of 20 or 21, was as prosector at Bart's to John's former student John Abernethy. He became two years later (1827) assistant to the curator of Hunter's museum, William Clift, who had been Hunter's protégé and amanuensis at the time of his death. In 1835 he married Clift's daughter, and in 1842 became Joint Conservator of the Museum with his father-in-law, and Conservator shortly later when Clift retired. The preparation of the great catalogues of John Hunter's collections was largely his. Furthermore, from 1836 to 1856 he was the first Hunterian Professor of comparative anatomy and physiology at the Royal College of Surgeons, with duties to present 24 lectures per annum illustrated by specimens from the collections. And he lived with the collections not only figuratively but literally, from 1835 until 1852 actually residing in apartments prepared for his use at the College of Surgeons.

It was within the period of the lectureship and of his residence at the College that he is said to have been influenced by the writings of Oken, one of the more extreme of the German *Naturphilosophen*; it was certainly during this period that he published his own principal theoretical views, in a book *On the archetype and homologies of the vertebrate skeleton* (17) which labors the concept that the vertebrate skeleton consists of a series of comparable segments, each of which is a modified vertebra. It might seem now that he was holding a fanciful view in maintaining for

instance that the maxillary bone represents the haemapophysis of the nasal vertebra, or the keel of a bird's sternum that of a thoracic one. But these were far less *outré* than many of the opinions expressed by Oken, who for example considered the whole animal kingdom to represent a single organism.

Owen's transcendentalism was short-lived in England; in 1858, just ten years after the publication of Owen's book *On the archetype*, Huxley completely demolished in his Croonian Lecture (18) the vertebral theory of the skull, for once and for all. But Owen's speculations on the archetype of the vertebrate skeleton were in no way his sole preoccupation, and after the delivery of Huxley's Croonian Lecture as well as before Owen devoted his primary efforts to the study of hard anatomy, anatomy which dealt with hard bones, hard teeth, hard shells, hard fossils, not ideas. Even Huxley, who distrusted him as a person as heartily as he disapproved of him as a transcendentalist, gave full credit to the value of his anatomical research: "The historian of comparative anatomy and palaeontology will always assign to Owen a place next to, and hardly lower than that of Cuvier . . . . It was not uncommon to hear our countryman called 'the British Cuvier,' and so far, in my judgment, the collocation was justified, high as the praise it implies" (19); then after some disparagement of Owen's "philosophical anatomy," Huxley concludes that "whatever view is taken of Sir Richard Owen's speculations . . . his claims to a high place among those who have made great and permanently valuable contributions to knowledge remain unassailable" (20).

I submit that Owen succumbed to seduction by transcendentalism in only one or two books, instead of becoming immersed in abstraction to the exclusion of all factual anatomy, in large part because of his training in the Hunterian tradition, of his experience in the Hunterian museum, of his work with the Hunterian specimens in his hands and his eyes and his mind. Romanticism often includes an element of other-worldliness; Hunter's specimens could hardly have been more exclusively of this world, and their substantiality and Hunter's solid treatment of them affected not only Owen but those who gave ear to Owen. While Owen's book *On the archetype* surely exerted some influence in England it was far less than the effect of comparable writings in *Naturphilosophie* on the Continent. This, as so much else, we owe to the Hunters, whose type of contribution assured that British anatomy escaped the perversion and adulteration it might otherwise have suffered.

It is not to the Hunters alone that this good fortune of British anatomy is to be attributed, of course the philosophical conditions were favorable in Britain for their kind of work and for that of their successors. But this in no wise minimizes their accomplishment; it was they, and not Locke and Berkeley and Hume (21) who enlarged the horizons of human and comparative anatomy and physiology. We started this evening by saying that we derive some of our ideas from them. Surely we inherit from them some of our modes of work as scientists; and if their voices speak to us clearly across two centuries, undistorted by pseudoscientific aberrations, this we owe to the vigor and the strength and the intellectual power with which they thought and worked.

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(17) Owen, R.: *On the archetype and homologies of the vertebrate skeleton*, John van Voorst, London, 1848.

(18) Huxley, T. H.: "On the theory of the vertebrate skull," *Proc. Roy. Soc.* IX, 381–457 (1857–59; Croonian Lecture delivered 17 June 1858).

(19) Huxley, T. H.: "Owen's position in the history of anatomical science," in Owen, R.: *The Life of Richard Owen*, John Murray, London, 1894, II, 312. Huxley was a little less mellow 36 years before when he wrote to Hooker: "What a capital title that is they give him of the *British* Cuvier. He stands in exactly the same relation to the French as British brandy to cognac." (Huxley, L.: *Life and letters of Thomas Henry Huxley*, D. Appleton and Company, New York, I, 172.)

(20) Huxley, T. H.: "Owen's position in the history of anatomical science," in Owen, R.: *The Life of Richard Owen, op. cit.*, II, 332.

(21) Mrs. John Hunter was a cousin of David Hume's, see Hume, D.: *The Letters of David Hume*, Clarendon Press, Oxford, 1932, II, 324.

John Redman (1722-1808): Medical Preceptor of Philadelphia*

By WHITFIELD J. BELL, JR.† PH.D.

IN HIS dark broad-skirted coat, his German jackboots, and a hat that flapped before and was cocked up smartly behind, mounted on a fat little swish-tailed horse, Dr. John Redman, president of the College of Physicians of Philadelphia, must have struck some of his fellow-citizens in 1800 as a curious survival from an earlier, primitive age.[1] To most of his professional colleagues, many of whom could not remember the time when Redman was fully engaged in active practice, he was a venerable relic who had known some of the first settlers of Philadelphia and had practiced medicine in the city before there was a hospital or anyone even dreamed of a medical school. At the opening of the nineteenth century he was in fact a very old man who had viewed the practice of medicine in Philadelphia through sixty years, seen medicine and the medical profession change, and helped make some of the changes. Odd though he may have seemed in his old flapping coat and full-bottomed wig, no one who knew John Redman laughed when he cantered by. To them—his patients, his colleagues, his co-religionists of the Presbyterian Church—he was the doyen of the medical profession in Philadelphia.

Born in Philadelphia on February 27, 1722,

DR. JOHN REDMAN
[From a picture in The Ridgway Library]

educated at William Tennent's Log College on the Neshaminy, young Redman was apprenticed to able but ill-humored Dr. John Kearsley, Sr.[2] He was thus a member of that generation which saw far-reaching changes in the education of doctors and the status of physicians. When the second third of the eighteenth century opened, all but a handful of physicians in America were either native Americans trained as apprentices to older doctors, or else were self-taught; or they were men recently come from Europe, most of them

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[1] John F. Watson, *Annals of Philadelphia, and Pennsylvania, in the Olden Time* . . . (3 v., Philadelphia, 1881) II, 382. Everyone interested in Redman must be indebted to the researches of Dr. William N. Bradley of Philadelphia; his notes, including copies of many of Redman's letters, carefully organized and neatly mounted in two great volumes, are in the College of Physicians of Philadelphia. A painting and a silhouette of Redman are also in the College.

[2] [Benjamin Rush], "Memoirs of the Life and Character of John Redman, M.D.," *Philadelphia Medical Museum*, V (1808) [49]–[56], is the principal source of biographical data, but needs to be used with caution, especially on Redman's views on practice. Rush wrote the obituary in *Poulson's Daily American Advertiser*, March 23, 1808. See also William S. Middleton, "John Redman," *Annals of Medical History*, VIII (1926) 213–223.

of dubious qualifications, many of them adventurers and quacks, who stayed a year or two and then moved on. Native-born Americans had not yet begun to go abroad for medical training, and nowhere in America was formal instruction offered.

Thirty years later much of this had changed. Then the leaders of the profession in America, especially in the middle and southern colonies, were men with degrees from Edinburgh, Leyden, or Rheims. Physicians with such training strengthened and improved the quality of the apprenticeship system, which remained the common pattern of medical instruction. In several colonies and cities medical societies were formed to guard and raise the standards of the profession and to exchange medical knowledge. A few individuals, like the elder William Shippen, experienced the changes in a personal way: as a drug seller in 1730 he had advertised himself simply "William Shippen, Chymist;" within twenty years he joined Kearsley, Thomas Graeme, Phineas Bond and six others in issuing a statement on behalf of "the practitioners of physic," and he was "Doctor" Shippen thereafter.[3] And in 1765 John Morgan and William Shippen, Jr., products of the apprenticeship system but also graduates of Edinburgh, established at the College of Philadelphia the first regular medical school in British North America.

Having completed a rigorous apprenticeship with Kearsley, probably in 1743 or 1744 (he was still an apprentice on July 3, 1742, when he purchased a copy of Horace at Benjamin Franklin's New Printing-Office),[4] provided with a letter of recommendation from his master, Redman left Philadelphia and commenced to practice in Bermuda. After a short time, however, with an inheritance from his father and a loan from Chief Justice Allen, perhaps on advice from Phineas Bond, who had studied in Scotland in 1742, he enrolled at Edinburgh University in October 1746. The great age of the Edinburgh medical school was just opening; and Redman was in the first generation of Americans to study there. He attended the lectures of Alexander Monro *primus* on anatomy and physiology and those of Charles Alston on materia medica, probably attended also clinical lectures at the Royal Infirmary, which John Rutherford inaugurated this year.[5]

The second winter, 1747–1748, Redman spent at Leyden, whose university still glowed from the luster Boerhaave had given it. Here Redman studied anatomy, surgery, and midwifery under Boerhaave's student and collaborator, Bernhard Siegfried Albinus; and medicine with Jerome David Gaubius, Boerhaave's successor in the chair. For his dissertation Redman presented a subject in obstetrics—miscarriage. He dedicated it to Kearsley and Judge Allen and closed it with a prayer: "God grant that my studies and labors may be directed to the glory of His name, and to the welfare of my neighbors." Albinus was his sponsor in the final examination, and Redman received his diploma as a doctor of medicine on July 15, 1748.[6]

Both at Edinburgh and Leyden, however, Redman's work was bookish and largely theoretical. For practical experience and observation Redman visited the Paris hospitals, possibly in the spring of 1748; and in the winter of 1748–49 he walked the wards at Guy's in

[3] *Pennsylvania Gazette*, May 18, 1749. The others were Christopher Witt, Lloyd Zachary, Samuel Preston Moore, Peter Sonmans, Richard Farmer, and John Kearsley, Jr.

[4] Benjamin Franklin, Ledger D, 1739–1748, 157, American Philosophical Society.

[5] His notes of Alston's materia medica are in the College of Physicians, those of Monro's anatomy and physiology in the National Library of Medicine (formerly Armed Forces Medical Library), Cleveland, O. A list of students and apprentices made by Monro gives the name of J. Redman as paying a fee of three guineas on October 29, 1746. L. W. Sharp to W. N. Bradley, August 10, 1948, Bradley Collection, I, 53-A.

[6] John Redman, *Dissertatio medica inauguralis de Abortu* (Leyden, [1748]). The Album Studiosorum at Leyden shows that Redman enrolled as a student October 6, 1747. Curators of the University to W. N. Bradley, August 17, 1948, Bradley Collection, I, 53-C. His diploma is now in the College of Physicians.

London. From the attending physicians of that ancient foundation he received a testimony to his "great application."[7] In London a friend gave him a copy of Sydenham's works; on the flyleaf the donor inscribed the lines from Pope's *Temple of Fame* which end:

Unblemish'd let me live or die unknown;
O, grant an honest fame, or grant me none![8]

In the spring or summer of 1749 Redman returned to Philadelphia; in November he purchased a Pennsylvania fireplace from Franklin;[9] and, thus reestablished in his native place at the age of 27, he left it seldom, and never for a long time, during the remaining sixty years of his life.

Within three years Redman acquired such a reputation in Philadelphia that, with Thomas Graeme, Thomas Cadwalader, and Charles Moore, he was asked to join Thomas and Phineas Bond and Lloyd Zachary as a consulting physician in the newly-established Pennsylvania Hospital.[10] When Benjamin Rush came as an apprentice to his house and shop in 1761, John Redman was said to have enjoyed for ten years one of the largest medical practices in the city.[11] Though for his health's sake he eventually gave up obstetrics and, some time after 1765, surgery as well,[12] Redman's income was substantial. He managed his property carefully, lived in great comfort, with a house in North Second Street and a country place a few miles from town,[13] and retired after thirty years' practice. He kept his shop, however—Washington bought some articles there before returning to Mount Vernon in 1797; and when he was past eighty he was testing a new Indian herb and joined his colleagues in a public recommendation of vaccination as "a certain preventive of the small pox."[14]

Such a rush of business made it necessary for Redman to accept apprentices. Aspiring students, on their part, looked on Redman's shop as one of the best places in the city to receive good instruction and varied medical experience. He never took more than two apprentices at a time, sometimes had but one—a limitation which, though it made Redman work more, doubtless made his students work harder too, and so promoted their education. Rush, who was recommended to Redman by President Samuel Davies of Princeton, remembered that in the five and a half years of his apprentice-

[7] [Rush], "Memoirs," *loc. cit.*, [49]–[50]. The certificate is dated February 21, 1748/9. Two passports for "Le Sieur Jean Redman natif d'amerique...etudian en medicin allant en hollande," dated May 30, 1748, are in possession of a descendant, Travis Coxe, Sugarloaf, Pa.

[8] The volume is *Opera Medica* (Geneva, 1716); Redman presented it to the College of Physicians. The inscription is dated Febraury 16, 1748/9. Almost forty years later Redman used similar terms in speaking of himself in his inaugural address to the College of Physicians in 1787. He had never had, he asserted, "great desires of exaltation above the middle state, nor higher ambition to conduct therein rather with integrity and usefulness than eclat." W. S. W. Ruschenberger, *An Account of the ... College of Physicians of Philadelphia* ... (Philadelphia, 1887) 180.

[9] Franklin, *op. cit.*, 157

[10] Thomas G. Morton and Frank Woodbury, *History of the Pennsylvania Hospital* (Philadelphia, 1895) 28.

[11] Benjamin Rush, *Autobiography* ... (George W. Corner, ed., Princeton, 1948) 38.

[12] In the certificate he gave his apprentice Samuel Treat on September 1, 1765, Redman declared that for nearly four years the young man had been "constantly employed in the practice of Physic and Surgery under my care ..." Stephen Wickes, *History of Medicine in New Jersey* ... (Newark, 1879) 102.

[13] Redman to Rush, April 4, 1767, speaks of the building of his country house. Rush Mss., XXII, 10, Library Company of Philadelphia. George Washington drank tea there July 9, 1787. *Diaries* (4 v., Boston, 1925) III, 227. See also Redman to Mrs. Ferguson, June 6, 1776, Redman to John Nicholson, October 15, 1799, Historical Society of Pennsylvania, and Redman to [ ], July 25, 1772, manuscript in possession of Captain Frank L. Pleadwell, Honolulu, typescript in Bradley Collection, II, 209. Redman's estate was valued in 1811 at $43,042.48. "Account of the Executors of the Will of John Redman, 1811," Historical Society of Pennsylvania.

[14] Rush to John Redman Coxe, January 16, 1796, L. H. Butterfield, ed., *Letters of Benjamin Rush* (2 v., Princeton, 1951) II, 769; Redman to Rush, September 25, [1804], Rush Mss., XXII, 9; Cecil K. Drinker, *Not So Long Ago* (New York, 1937) 101–102; "Washington's Household Account Book, 1793–1797," *Pennsylvania Magazine of History and Biography*, XXXI (1907) 346.

ship he was absent from his master's business only eleven days "and never spent more than three evenings out of his house." Rush kept Redman's books, and when the older man was ill or out of town, the whole burden of his practice fell on him.[15]

Redman gave his pupils Boerhaave and Sydenham to study, had them abridge Van Swieten's Commentaries, encouraged them to keep a commonplace book to record observations of his practice. He let young Benjamin Duffield copy his notes of Monro's lectures; his grandson John Redman Coxe filled a notebook with copies of his miscellaneous letters and papers on yellow fever.[16] Rush spoke gratefully and warmly of his master as unrivalled "in everything that's good. I have experienced kindness from Dr. Redman I had little reason to expect," he continued. "I have ever found in him not only the indulgent master but the sincere friend and tender father."[17] Benjamin Waterhouse, writing in 1790 when he was a professor in the Harvard Medical School, assured him that his kindness sixteen years before was "still fresh in my memory."[18]

Redman reciprocated the tenderness of his apprentices and young friends. He rejoiced in their success, advised and encouraged them like a wise father, called them with affectionate pride his "professional children." "As it is no small gratification to my ambition, to have been instrumental in initiating you and other young gentlemen of reputation into that part of life which is most important," he assured one, "so it is & will be one of the greatest joys of my increasing years, & declining age, to see you prosper. . . ."[19] Each year he sent Rush—his "justly respected, & much esteemed Christian friend & medical son"—a friendly Christmas or New Year's greeting.[20]

Boerhaave and Sydenham were Redman's principal guides in theory and practice.[21] It is perhaps significant that he presented a copy of the works of each to the library of the College of Physicians. Their doctrine, which put the patient at the center of every medical situation, appealed to Redman's personal humanity; he appreciated their practical good sense; like them, accepted truth where he found it. His master John Kearsley had once found the hint of a successful treatment in an old author. "And may not this be a hint also to us," he asked his brethren in the College of Physicians,

> not to slight or neglect the practical observations of even antiquated authors, because they do not quadrate with the more enlightened theories of the present day? Yea, tho' we may with some reason . . . smile at their mode of theorizing upon them, let us rather . . . give them all the credit we can, for their great and often painful attention to what might conduce to the progress of the

[15] Rush, *Autobiography*, 37–38; Rush to Ebenezer Hazard, March 19, 1765, Butterfield, *op. cit.*, I, 11.

[16] The notebooks of both Duffield and Coxe are in the library of the College of Physicians of Philadelphia.

[17] Rush to Ebenezer Hazard, May 21, 1765, Butterfield, *op. cit.*, I, 13. At the time when Rush wanted Redman's influence to get him the appointment as professor of chemistry in the new medical school of the College of Philadelphia, however, the younger man spoke angrily of his master. Rush wanted to be elected while he was still a student at Edinburgh; Redman thought he should wait until he returned home, advised him to bring with him a certificate of his qualification in chemistry, "as it will be more honorable to you, and the College, to ground their election thereon." There is no evidence that Redman did not support Rush's candidacy on these terms, and Rush was elected to the chair. Redman to Rush, May 12, 1768, [1768 ?], Rush Mss., XXII, 11, 19; Rush to John Morgan, January 20, July 27, 1768, Butterfield, *op. cit.*, I, 49–50, 62.

[18] Benjamin Waterhouse to Redman, December 20, 1790, Ms. Archives, 145, College of Physicians of Philadelphia.

[19] Redman to Rush, April 4, 1767, Rush Mss., XXII, 10.

[20] Same to same, December 21, 1782, January 1, 1796, January 5, 1802, *ibid.*, XXII, 21, 13, 17.

[21] [Rush], "Memoirs," *loc. cit.*, 51–52. Mrs. Grace Growden Galloway, a friend of the Redmans before the Revolution, recorded a dissenting view. Ill, she sent twice for Redman, "but he made excuses & wou'd not come." Next day, when he did visit her, he displayed "such Contempt & disrespect that I wish I had not sent for him—he would scarce hear what I had to say." But Mrs. Galloway was overwrought. Raymond C. Werner, ed., "Diary of Grace Growden Galloway," *Pennsylvania Magazine of History and Biography*, LV (1931) 81.

healing art and the benefit of mankind; and but for which possibly we might not have yet been so far advanced in successful practice as we now are, whatever we might have been in diversity of theories. Is not old Sydenham an eminent instance of the truth of the above observation?[22]

According to Rush, Redman subsequently modified this moderate therapeutic practice. When William Cullen and John Brown called some of Boerhaave's doctrines into question, Redman considered their arguments and adopted some of their views and methods. Still later he asked to read Rush's "whole course [of lectures on medicine] regularly thro' " for they pleased him "much."[23] Redman, Rush asserted in the obituary he wrote, "considered a greater *force* of medicine necessary to cure modern American, than modern British diseases, and hence he was a decided friend to depletion in all the violent diseases of our country." If in fact Redman ever held these views, he held them at the end of his life. While he was one of Philadelphia's busiest doctors he practiced Hippocratic medicine. In the yellow fever epidemic of 1762, for example, he used saline purgatives successfully; in the more widespread epidemic of 1793 he seemed still to prefer them to bleeding and heroic doses of calomel and jalap.

Like all good doctors, Redman appreciated that the patient's mental state is an important condition of successful treatment. In the sick room, Rush remembered, Redman "suspended pain by his soothing manner, or chased it away by his conversation," which was grave or gay, instructive or anecdotal as the nature of the patient's illness and psychological condition indicated. A woman whom he attended during a fatal sickness told one of her friends that death had nothing terrible in it when Dr. Redman spoke to her about it. (S. Weir Mitchell envied Redman the secret of this "anaesthetic kindness."[24]) When his patients kept well, Redman visited them two or three times a year all the same. Treating female patients, like Mrs. Elizabeth Graeme Ferguson, for example, he not only prescribed medicines, but often also wrote them letters, paid them visits which seemed merely social, counselled them on personal and business affairs quite unconnected with health and disease. "By no means" should Mrs. Ferguson sell the mansion house, he advised strongly in 1782; "and . . . you ought to keep two hundred acres with it."[25]

Redman's practice, like his whole view of life, was deeply influenced by an invincible religious faith. If Redman's appreciation of the moral causes of physical conditions made him aware that the strongest medication may sometimes prove ineffective, his Christian conviction that God has ordained all things made him cautious in initiating radical treatments or claiming credit for the cures.

John Redman's name appears on the rolls of the Second Presbyterian Church in Philadelphia first in 1744, as *juvenis*—a young man. Soon after he established himself permanently in the city, he assumed increased responsibilities for the temporal work of the church. He was a member of the committee of the congregation after 1760, a member of the committee appointed in 1761 "to wait on Robert Smith Carpenter for a plan for the Steeple," and one of the collectors of pew rent. When the Second Church was incorporated, Redman was elected a trustee, he was subsequently vice president, and from 1786 to 1803 he served as president of the Consistory.[26] He became an

[22] Redman, *An Account of The Yellow Fever as it prevailed in Philadelphia in the Autumn of 1762* . . . (Philadelphia, 1865) 39–40. The original manuscript is in the College of Physicians of Philadelphia.

[23] Redman to Rush, January 1, 1796, Rush Mss., XXII, 13.

[24] S. Weir Mitchell, "Commemorative Address," College of Physicians of Philadelphia, *Transactions*, 3rd ser., IX (1887) cccxlv.

[25] See, for example, the letters of Redman to Mrs. Elizabeth Graeme Ferguson, [April, 1773], May 3, 1773, June 6, 1776, February 26, 1782, in Historical Society of Pennsylvania. Other data on Redman's practice may be found in Drinker, *op. cit.*, 95 *et passim*.

[26] Second Presbyterian Church, Congregational Minutes, I, *passim*; Minutes of the Corporation, I, II, *passim*, typescripts in Presbyterian Historical Society, Philadelphia.

elder in 1784, for many years made an annual gift for the relief of poor women of the church, was a constant reader of devotional literature.[27] In this his taste ran to piety rather than disputations or dogmatic theology; he hailed the popular evangelical preacher and writer Elhanan Winchester, for example, a Baptist with Universalist leanings, as "our *Theological Newton*."[28]

Such constant service to the church and contemplation of religious purposes through half a century was at once an expression of, and a stimulus to, his faith. When the church's minister, Ashbel Green, vacationing in Princeton in September 1797, debated whether to return to Philadelphia, where yellow fever was raging, Redman addressed him not as a physician but as a fellow-Christian:

> Mr. Falconer & myself still continue to conceive it to be your duty to venture, and beside other reasons offered to yourself before, we think that if it be deemed improper or unjustifiable for medical doctors, & natural parents to quit us at such times, it is equally if not more so, for our spiritual fathers to desert us alltogether, or at least not occasionally to aid the remainder of their flock who cannot, or dare not emigrate, in their worship, & improvement on the present calamitous occasion. Nevertheless we do not pretend to dictate, much less to censure others, but leave them to judge for themselves, withall praying spiritual light, & supernal direction & strength may be afforded them therein.[29]

Like an ancient Christian, John Redman looked forward to death. Doubtless the poor state of his health from middle age onward made him constantly aware of bodily weakness and the uncertainties of life. But there was nothing gloomy in his looking on "that Grim old *Gentleman*," as he once called death. On the contrary, he spoke of it, Rush declared, as other men speak of going to bed or making a journey to a pleasant, distant country.

This stalwart Christian faith had some clearly definable effects on Redman's medical practice. Quite as much as his Hippocratic good sense, it seems to explain Redman's constant reminders to students and colleagues that God rules and overrules the physician. He was skeptical of systems and theories, was no enthusiast for general reforms, not only because as a man of science he was conscious of the limitations of human knowledge, but because as a Christian he believed that God in his providence has decreed life and death, pain, suffering, and health for each man. When Rush wrote him excitedly of the expansive ideas he was getting from his Edinburgh teachers, Redman reminded the young man that "however pleasing the prospect may be of returning to our friends fill'd with knowledge and qualified to be usefull, it is only a possession of the one thing needfull, that can make us happy in ourselves, a real blessing in our generation;" and that "one thing needfull," in Redman's view, was not knowledge of medicine but faith in God.[30] Similarly, when John Morgan proposed, for the purpose of raising the standards of practice in this country and perhaps to carry on physiological researches, to practice medicine but not surgery and to sell no drugs, Redman addressed him a sermonette on Christian charity, clearly implying that a physician ought to "be every hour engaged in doing good to rich & poor, relieving the distresses of poor suffering fellow mortals, and perhaps receiving daily blessings of those who are ready to perish. . . . No life can be happy or pleasing to God but what is usefull to man."[31] And he expressed like ideas

[27] Second Presbyterian Church, Consistory Book, 1744/5–1798, *passim*, typescript, Presbyterian Historical Society; Isaac Snowden and others to Ashbel Green, December 25, 1793, Historical Society of Pennslyvania.

[28] Rush to Elhanan Winchester, November 12, 1791, Butterfield, *op. cit.*, I, 611.

[29] Redman to Ashbel Green, September 20, 1797, Historical Society of Pennsylvania.

[30] Redman to Rush, April 4, 1767, Rush Mss., XXII, 10.

[31] Redman to [John Morgan], March 13, 1764, draft, Gilbert Collection of Ms. Letters, III, 354, College of Physicians of Philadelphia.

in his inaugural address as president of the College of Physicians in 1787.[32]

As he withdrew from practice and turned his mind increasingly to religious contemplation Redman seems almost to have come to accept disease as a part of the order of the universe, which it verged on impiety to alter. The yellow fever, Redman told Mrs. Elizabeth Drinker quietly in 1798, "is progressing, and will progress; 'tis according to the nature of things at this season of the year;" and he talked of going into the country with his wife and daughter.[33] When Mrs. Redman, his "Fellow Traveller in the thorny mazes of time," became ill, he half apologized for asking Rush to visit her:

> And though I hope this sickness is not unto death but for the glory of God; yet after a union of thirty years, the most distant prospect of a separation . . . makes one shudder, especially in the present circumstances. And though to depart hence and be with Christ I know would be far better for her, but to remain longer here . . . I hope would be better for me; nevertheless . . . as all prudent means are rational . . . a visit from you will be very acceptable, and much oblige your old (paternal) friend.[34]

Another medical consequence of Redman's Christian resignation was to discourage any inclination he might have had to carry on systematic observations or investigation into medical problems. In a short published letter he described his method of inoculating against small pox, but this was called forth by a desire to combat secrecy in medicine and probably would not have been written otherwise. His paper on the yellow fever of 1762, written at the time of the disastrous plague of 1793, was not a systematic study, but a collection of observations, an account of treatments the doctors tried, based upon his old daybook and the recollections of "an ancient woman and others" whom Redman remembered he had attended.[35] Redman was, in short, as Benjamin Smith Barton complained, one of "the *large* number of those practitioners of the healing art, who mix, for years, with the sick, and who scarcely leave behind them one important memorandum of what they have observed, in regard to the nature of the diseases, or the effects, whether good or bad, of medicines." The capacity for making accurate observations, Barton conceded, is not common even among physicians. "But every physician, possessed of a good understanding, has it in his power to augment the mass of MEDICAL FACTS, and thereby to extend the certainty and usefulness of the most important of all the sciences."[36]

John Redman was the first president of the College of Physicians in 1786. He was not the founder of this medical society—the College was the work of others; and though he was one of the oldest members, he was not the most famous. Morgan, Shippen and Rush were better and more widely known, but none of these men could have been elected head of a Philadelphia medical society without dividing it at its birth. Redman on the contrary, a successful practitioner, wise and tolerant, was held in esteem by all. He was reelected president annually until, at his own request, he was allowed to retire in 1804.[37]

As president of the College Redman reigned rather than ruled. He presided at regular meetings when he was well enough to attend; he called special meetings when the fellows petitioned for them or the governor of the Commonwealth requested one; he received communications addressed to him as president, passed them over to the secretary to answer, and signed the replies after they were drafted. He rejoiced publicly that the vice presidents of

[32] Ruschenberger, *op. cit.*, 179–183.

[33] Drinker, *op. cit.*, 133; Redman to Ashbel Green, September 14, 1798, College of Physicians of Philadelphia.

[34] Redman to Rush, February 25, 1782, Rush Mss., XXII, 12.

[35] John H. Powell, *Bring Out Your Dead* (Philadelphia, 1949) 87–89.

[36] *Philadelphia Medical and Physical Journal*, III, pt. 1 (1808) 189–190.

[37] Redman to Vice President and Members of the College of Physicians, July 2, 1804, Ms. Archives, 429; Redman to Thomas Mifflin, September 26, 1799, Historical Society of Pennsylvania; Drinker, *op. cit.*, 127.

the College during these years were younger men and vigorous.[38]

Redman's civic activity, like his service to the College, was unspectacular. He was a trustee of the College of Philadelphia for forty years from 1751, and as a trustee of the College of New Jersey at Princeton from 1761 to 1778 he seems to have taken a lively interest in the fortunes of Nassau Hall. In Philadelphia he was a member of the American Philosophical Society, the Agricultural Society, and the Prison Society. In none of these, however, did he take so active and responsible a role as he did in his church; and it is even doubtful whether he was much interested in science, he certainly had no farm, and though he was a benevolent man he was in no sense a social reformer.[39]

One is left to wonder what the source of his reputation was; why, for example, despite repeated absences and constant disclaimers of capacity, the physicians of Philadelphia elected him president of the College year after year? What made him by general assent the Nestor of the medical profession in Philadelphia?

In the first place John Redman was an able physician, the teacher of able men—Morgan, Rush, and Wistar, Ralph Assheton, Samuel Treat, and Isaac Cathrall—and he was devoted to his profession. Rush preserved a toast which Redman proposed on some occasion:

> The dignity & success of the healing art—and long health, competent wealth & exquisite happiness
>
> To the individual practitioner, who makes the health, comfort & happiness of his fellow mortall one of the chief ends & delights of his life; and acts therein from motives that render him superior to all difficulties, he may have to encounter in the pursuit thereof.[40]

The man who can offer that toast *is* at the head of his profession.

Another reason for Redman's reputation has been suggested by W. B. McDaniel, 2d. Redman may have owed "the robes, at least, of power" to the "sedulously cultivated image of himself as an aged and infirm patriarch." From the time he was forty John Redman spoke constantly in his letters of his age, his weakness, his sickness, pain and forgetfulness in tones which could only produce concern, sympathy, even love.[41] The physicians were not alone in reacting as Dr. McDaniel has suggested they may have done—the trustees of the Second Presbyterian Church treated Redman in the same way, probably for the same reason.

Finally, of course, Redman's contemporaries respected him because he was so patently a man of integrity and good will. His manners were antique; a new generation of physicians, taught by Rush, thought him too cautious in practice; and his gaze was too steadily fixed on heaven to make him an apt ally of those who were doing the world's work in Philadelphia. But there was nothing grasping, proud, or contentious about Redman. Only goodness came from him even as a young man, for if his temper overcame him and he spoke sharply to an apprentice, he never failed to apologize

[38] Redman, Address on his reelection as president, [1791], Ms. Archives, 393. In his official capacity Redman sent the President of the United States two copies of the proceedings of the College relative to contagious diseases. In reply John Adams asked Redman to assure the College that he would "be always ready to concur in any proper constitutional measures which the Legislature of the United States, may determine to adopt for preventing the Introduction of Contagious Diseases into the Ports of the United States." Adams to Redman, February 3, 1798, Ms. Archives, 349.

[39] Henry Phillips, Jr., "Early Proceedings of the American Philosophical Society...1744 to 1838" (*Proceedings*, XXII [1885]) *passim*; Philadelphia Society for Promoting Agriculture, *Memoirs*, VI (1939); *Constitution of the Philadelphia Society for Alleviating the Miseries of Public Prisons* (Philadelphia, 1821) 12.

[40] Redman, [Toast], Rush Mss., XXII, 8.

[41] See the suggestive article by W. B. McDaniel, 2d, " 'Your Aged Friend and Fellow Servant, John Redman,' " College of Physicians of Philadelphia, *Transactions & Studies*, 4th ser., IX (1941) 35–41. Someone, possibly Rush, in a letter of August 23, 1782, reminded Redman that he should count his blessings, that he had escaped all kinds of early death, had health and reason, reputation and prosperity. *Evangelical Intelligencer*, n.s., II (1808) 326–329.

promptly. As an old man he could praise Thomas Paine, and thought it

> strange . . . & wonderfull, that even the madness . . . of the people in France, should be made the means of accomplishing the grand purpose of their own liberation, liberty, & political happiness, probably sooner, & possibly much firmer than would have been done by the exercise of their sober reason & senses . . . .[42]

In an age of loud and jealous Hippocrats, Redman was remarkable for sound sense, humility, charity, and quiet confidence. For these qualities he was respected by all and liked by many, and most men cheerfully allowed him the title he had assumed with modest but affectionate pride in 1787—that of the professional father of the physicians of Philadelphia.

[42] Redman to Rush, January 1, 1793, Rush Mss., XXII, 13.

Acknowledgment: This study was published in part as "John Redman, Medical Preceptor, 1722–1808," in *The Pennsylvania Magazine of History and Biography*, LXXXI: 157–169, April, 1957. For permission to reprint it, we are indebted to Mr. Nicholas B. Wainwright, editor of the *Pennsylvania Magazine*.

Letter on Inoculation, 1760

By JOHN REDMAN, M.D.

Note by WHITFIELD J. BELL, JR., PH.D.

SECRECY was one of the conditions impeding medical progress in the Eighteenth Century. Regarding their prescriptions, instruments, and techniques as a skilful artisan might regard his method of dyeing cloth, some medical practitioners refused to reveal not only their "cures" for cancer and the stone (with good reason) but also their treatment of patients undergoing inoculation against smallpox.

One of those who opposed secrecy in medicine was Benjamin Franklin. Living in London, where he was agent of the colony of Pennsylvania, he asked the distinguished William Heberden in 1759 to write a set of instructions in such plain, unscientific language that any literate person might perform inoculation and conduct a patient successfully through the resultant disease. To Heberden's "plain instructions" Franklin wrote a preface showing, by statistics drawn from the New England smallpox epidemic of 1752, how much safer inoculation was than smallpox taken in the "natural way."

A large number of the Franklin-Heberden pamphlets—Franklin's answer to the inoculators' secrecy—was sent to America for free distribution.[1] In a letter printed in the *Pennsylvania Gazette* of June 26, 1760, a New Jersey practitioner who signed himself only "Americanus," warmly endorsed this pamphlet "as containing some of the best general Rules for the Preservation of our Fellow Creatures from the dismal and fatal Effects of that frightful Distemper;" and he added some specific directions received from the elder Dr. William Shippen of Philadelphia and drawn from his own experience.

The next week a second letter on inoculation was printed in the *Gazette*. This letter too had been written by a physician—"J. R.;" originally prepared for the short-lived *New American Magazine* of Woodbridge, N. J., an abstract of it was sent to the printer of the *Pennsylvania Gazette* ostensibly by a friend of the author. J. R.'s letter consisted of two parts. In the first, which was strictly medical, the author set forth his prescriptions for preparing patients for inoculation and caring for them during the progress of the disease. Like Americanus, J. R. went into more detail than Heberden; unlike the English physician's, his prescriptions required an apothecary and his patients, doubtless, the attendance of a physician. The second part of J. R.'s letter was an attack on the secrecy of the inoculators. Where Americanus however, had only expressed strong disapproval, J. R. appealed to the doctors to abandon secrecy, reveal their methods, and promote the happiness of mankind.

There are several reasons for believing that "J. R." was John Redman. In the first place, there is Rush's testimony: "About that time [1759]," he wrote in his account of medical practice in his student days, "Dr. Redman published a short defence of it [inoculation], and recommended the practice to his fellow-citizens in the most affectionate language."[2] J. R.'s letter is such a defence and recommendation. If it has hitherto eluded bibliographers that is probably because it was not separately published and Rush made a mistake of one year in dating it. In the second place,

[1] Henry K. Cushing, "Notes Suggested by the Franklin-Heberden Pamphlet of 1759," Johns Hopkins Hospital *Bulletin*, XV (1904) 276–285; Carl Van Doren, *Benjamin Franklin* (New York, 1938) 296.

[2] Benjamin Rush, *Medical Inquiries and Observations* (2nd ed., 4 v., Philadelphia, 1805) IV, 374.

the methods J. R. outlined in his letter of 1760 are the methods John Redman followed when he inoculated Elizabeth Drinker's children two years later. Finally, J. R.'s literary style is like John Redman's: the former's appeal to religion and sentiment is characteristic of the latter, similar to the terms in which Redman addressed John Morgan on the proper principles of practice five years later.

The evidence is not irrefutable, yet it seems probable that the author of the letter on inoculation in the *Pennsylvania Gazette* of July 3, 1760, was in fact John Redman.

June 10, 1760.

Sir,

At your Request, I now send you my Method of preparing Patients inoculated for the Small-pox; which I chearfully comply with, not only to gratify your benevolent Disposition, but that I wish every successful Method herein may be as extensively known as possible.

I shall first mention the Medicines, in the Form prescribed, and then the Manner of administring them, with some other necessary Circumstances.

Take of Calomel, finely levigated, two Parts; Sulphur Aurat. Antimonii, one Part; and with a strong Solution of Gum Arabic, or Tragacanth, make into a Mass of Pills; which, for Distinction-sake I will call the Mercurial or Antimonial Pill.

Take of Stib. Nitrat. or unwashed Diaphoretic Antimony, Cremor Tartar, Sal Polychrest, and Flor. Sulphur, of each equal Parts; mix and make a refrigerant Powder, of which 30 or 40 Grains is a Dose for an Adult.

Take the Powder of Jalap, Scammony, Stib. Nitrat. and Cremor Tartar, of each equal Parts, mix and make a purging Powder.

The Day before Inoculation give two Scruples of the purging Powder, with five Grains of Mercurius Dulcis, to Adults, and to others in Proportion to their Age. The Night after Inoculation give a Dose of the Mercurial Pill (which is ten Grains, or twelve, if robust, to an Adult, diminishing according to the Age, so as to give to one from nine to twelve Months two Grains) and repeat it three Nights successively. The Morning after the third Pill, give a second Purge; after which repeat the Pills two or three Nights, and then the Purge again. The Pill frequently purges or vomits the first Time of taking it. Every Morning, including the Day of Inoculation, give a Dose of the refrigerant Powder (except the Day the Purges are administred) continuing them till the Eruption.

Adults, who are very plethorick, should be bled on or near the Time of Inoculation, and also on the Day you expect them to be seized with the eruptive Fever, which is generally the 8th, tho' some few have been a Day or two later. But if not very plethorick, or under ten or twelve Years old, once bleeding, a Day or two before the Fever, may be sufficient. They should abstain entirely from animal Food, and all Kinds of Oil, Spice or Spirits, and all violent Exercise; but Vegetables and Acids they may use plentifully. They should not be closely confined, except when the Air is very cold and moist; and when the variolous Fever comes on, they should be kept rather cool than hot. Let their Drinks be cooling, acescent and laxative, especially Tartar Whey.

If they complain of their Mouths and Throats, give them a Teaspoonful of Flour of Sulphur, for two or three Times, instead of the refrigerant Powder.

As I was called to inoculate some under two Months, and finding that the Pill was full strong, even for those of six Months, I gave the following Powder, viz. Take of testacious Powder, and Nitrum Stibiatum, each Half a Drachm; of Cinnabar of Antimony and Calomel, each ten Grains, mix and rub them into a fine Powder, of which give eight Grains to a Child of six Months, and four or five Grains to one of six Weeks or two Months old: And to promote a little Puking, I add to their Purges, which should be Rhubarb and Calomel, a small Quantity of Sulphur Aurat. Ant. e.g. Half a Grain for one of six Months old.

Sometimes a universal Rash appears with the Fever, and alarms those concerned very

much; but it rather portends Good than Ill, and need not be regarded, unless attended with other known bad Symptoms, and then Venesection may be proper, even to Infants. I have generally used the Powder for Children in the form abovesaid, but have occasionally varied the Proportions a little. I have to some used only the Pills and Purges with equal Success. I am also fully satisfied, that it is a Matter of Indifference, whether the Incision in the Skin, and the infectious Lint placed therein, be large or small.

This, Sir, is the Method I have principally used ever since the Small-pox has appeared among us the last Time, with the most desirable Success; and which, I am assured, upon very sufficient Evidence, differs in nothing materially from the great Secret, so much talked of here, and in the neighbouring Provinces, yet so carefully and ungenerously concealed. The chief Difference being in their giving the Panacea Antimonii instead of the Sulphur Auratum, which last I prefer; and in their using only the Stibium Nitratum, and Cremor Tartar, equal Parts, as a Refrigerant: They also use the Flower of Sulphur more frequently, but I believe this is principally to prevent the Mercury from touching the Mouth, and so to conceal it the more; but I have had little Occasion hitherto to use it for that Purpose, tho' I think it a good Medicine, as a Preparative for the Small-pox.

As I had used my own Method to some Scores of Patients, before I was informed of theirs, and with at least equal Success, I have seen no Reason yet to alter it. If you see fit to communicate this to any of your Friends here or abroad, or to the Public, and by that Means the important Affair of Inoculation may be promoted, it will give me much Pleasure, and for which I desire no greater Reward, than that they would communicate as freely as they receive.—I took my Hints chiefly from Boerhaave and Hillary, and should have before this Time made them more public, but I waited to confirm them by a proper Number of Observations in my own Practice, and also was in Hopes some of those, who declared themselves possessed of a grand Secret, would have been generous enough to divulge it for the Benefit of Mankind; not knowing till lately how much better it might be than my Method above specified. But I have not failed to communicate it freely, where I had a proper Opportunity, and by that Means there are some practising it in different Parts of this and other Provinces, with amazing Success on great Numbers. Please to accept this as a Token of the sincere Regards of

Your much obliged Friend,
and humble Servant,
J. R.

If you should make this public, please to add the following Thoughts, which have often occurred to me on the Occasion.

We are certainly much obliged to every one, who has industriously endeavoured to encourage Inoculation, and improve the Manner of preparing the Body for the Small-pox, let their Motives have been what they will; if benevolent, so much the better; but if for Fame, or other private Ends, every Man has a Right to judge and act for himself; and for what is natural to Mankind in general, we should be tender of blaming any One in particular. The public Good had better be promoted by lower Motives than not at all: I had rather publish in such a Case, with selfish Views, than conceal for Profit only.

If any Thing I have said may contribute to the general Good of Mankind, or the Credit of the Profession, or prompt any to make public their Improvements in Inoculation, &c. I have obtained my End. But still I cannot help further urging those who have discovered any such Improvements generously and candidly to divulge them. Let us consider how great a Virtue is disinterested Benevolence; remember and imitate the Example of the Prince of Peace, who went about doing Good not only to the Good, but to the Unthankful; and forget not to practice the golden Rule of doing as we would be done by. Recollect, how when you have come to inoculate a Child, the distressed

Parent has met you bathed in Tears, dreading the Hand that is to sow the Seeds of Disease (so often fatal) in the Flesh of her tender Infant, shewing by her Aspect that nothing but absolute Necessity, and the almost certain Persuasion of Success, could have prevailed on her to do what her Conscience hardly allows. See with what Anxiety and Care she overcomes her own Tenderness, in forcing down the Antidote, and implicity follows every Direction that has a Promise of Success annexed. And when the pretty Babe begins to feel the dreaded Poison operate, how does every Look, every Word, every Action call on you for Comfort. But when the eruptive Fever is finished, and the promised Hopes confirmed, by a kindly Eruption of so few Pustules, that neither Life, Health, or Beauty are in Danger, but especially when the happy Crisis is performed, and the last well adapted Dose is administred, how does her Eyes and Tongue meet you with Gratitude, looking on you, under Providence, as the Preserver of her beloved Infant, now blessing the Hand and Heart she once thought almost cruel; while the Father chearfully and generously rewards your Skill, and the anxious Moments in which you sympathised with him, and thereby alleviated his. And now put yourself in the Place of either of those Parents, or of the Infant, and consider what Pleasure must it give to a generous Mind to bestow so much Happiness, and what you would think of the Man who could withhold such Aid and Pleasure from you; and further judge what Temper of Mind must he be of, that can refuse his Assistance, as far as possible, in such an Affair, whereby some fearing Want of proper Skill, or a Knowledge of the Secret, may be deterred altogether, and so exposed to take it in the natural Way. Consider of what extensive Use would such a Benevolence have been the last Year at Carolina, if timely Discovery had been made, while its Borders were ravaged by an Enemy, and its Towns and Garrisons ininfected by this cruel Disease; how much Comfort would it have yielded not to a few Persons only, but to a whole Province; and tho' others had reaped the Profit, a generous Mind would have had a Pleasure superior to any pecuniary Rewards.—If any really have a greater or more effectual Remedy against this Disease, and cannot be prevailed on to divulge the most latent Secrets of their Breasts in a Case of such Importance; may they nevertheless still go on and prosper for the Good of Mankind. I heartily wish them Success, and a plentiful Reward; but must remind them that the good Man (Mente conscia recti) will enjoy Pleasure in Poverty, from the Rewards of Virtue, while an obdurate Heart may indeed enjoy the Curse of an Estate, if not with Infamy abroad, yet with Remorse within, and justly.

Memoir of John Heysham Gibbon (1871–1956)*

By JOHN B. FLICK, M.D.

DR. JOHN HEYSHAM GIBBON, a past president of the College of Physicians of Philadelphia, and one of its most distinguished Fellows died March 13, 1956, at the age of 85.

Dr. Gibbon was born in Charlotte, North Carolina, on March 16, 1871, the fifth generation to graduate in medicine in a direct line of descent. His great, great grandfather was Dr. John Lardner of London whose son Lynford came to Philadelphia. It is interesting to note his sister, Hannah, married Richard Penn, youngest son of William Penn. Lynford became a Provincial Counsellor of Pennsylvania and was one of the organizers of the Assemblies in 1748.

Dr. Gibbon's great grandfather, John Hannum Gibbons, was born in Chester County, Pennsylvania, in 1759, obtained the Bachelor of Medicine degree from the University of Pennsylvania in 1782, Doctor of Medicine degree from the University of Edinburgh in 1786 and, returning to Philadelphia, was elected a Fellow of this College in March, 1788. For a number of years he delivered a course of lectures on the Theory and Practice of Medicine, apparently in a private capacity. He died in his middle thirties and was buried in Christ Church burial ground at 5th and Arch Streets, opposite the grave of Benjamin Franklin.

He left one son, John H. Gibbons, born in 1795, grandfather of the subject of this memoir, who graduated in medicine at the University of Pennsylvania but did not practice medicine. He devoted himself to scientific pursuits and became a well known mineralogist. In 1834, he was appointed assayer of the United States Mint at Charlotte, North Carolina. He married Catherine Lardner, daughter of William Lardner and granddaughter of Lynford Lardner. With this generation the "s" was dropped from the family name and he became John H. Gibbon.

His second son, Robert Gibbon, father of the subject of this memoir, graduated from Jefferson Medical College in 1847 and returned to Charlotte to practice, devoting himself particularly to surgery. Robert had two sons, Robert L. and John H., both of whom graduated from Jefferson Medical College. Robert L. returned to Charlotte. John H., the subject of this memoir, remained in Philadelphia.

Dr. Gibbon received his early education in public and private schools and in medicine at Jefferson Medical College where he graduated in June 1891. He served his internship at the Polyclinic Hospital and then spent three years as resident physician at the Pennsylvania Hospital.

Dr. Gibbon began the practice of medicine in Philadelphia in February, 1895.

Elected to Fellowship in the College of Physicians in 1899, he served at one time or another on the Alvarenga and Nathan Lewis Hatfield Prize and Lectureship Committees, the Committee on Directory of Nurses, the Committee on Entertainments and the Committee on the Weir Mitchell Oration. He was elected Councillor for five separate periods. In 1925 he was elected Vice-President and in 1928 President. He was an elected Censor of the College from 1935 until the time of his death.

Dr. Gibbon, from the start of his medical career, probably aspired to the practice of surgery. In 1896, he was elected Surgeon to the Out-Patient Department of the Pennsylvania Hospital. Always a horse lover, he soon acquired a smart gig which he drove to and from the hospital. Shortly after commencing practice, he was appointed assistant demon-

* Read before the College of Physicians of Philadelphia, 6 March 1957. Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

strator of anatomy at Jefferson Medical College and later demonstrator of osteology in the same institution, a position which he held for several years. His work in osteology may well have had something to do with an interest in fractures which was to come later and remain throughout his professional career. In 1899, he was elected Chief of the Surgical Clinic at the Jefferson Medical College Hospital under Dr. W. W. Keen, a position which he held until 1901 when he resigned to accept a Professorship of Surgery at the Philadelphia Polyclinic.

Already Dr. Gibbon was attracting attention as a teacher and a surgeon. By now he had contributed a number of articles to the surgical literature. In 1903, he was elected Surgeon to the Pennsylvania Hospital to succeed the late Dr. Thomas G. Morton. The same year he returned to the faculty of the Jefferson Medical College as an associate professor of surgery, a position which he held until elected to full professorship in 1907. For some years, Dr. Gibbon was Surgical Registrar at the Philadelphia Hospital, and held an appointment on the Surgical Dispensary Staff of the Children's Hospital. In 1900, he was elected Surgeon to the Bryn Mawr Hospital.

On September 2, 1901, Dr. Gibbon married Miss Marjorie G. Young, the daughter of the late Lieutenant-General S. B. M. Young of the United States Army, and Mrs. Young.

In the field of military service Dr. Gibbon's record was distinguished. During the Spanish-American War he served as First Lieutenant and Assistant Surgeon in the Third U. S. Volunteer Engineers, resigning when peace was declared to resume professional work in Philadelphia. On April 11, 1917, he was commissioned Major in the Medical Reserve Corps of the U. S. Army and attached to Pennsylvania Base Hospital 10, which subsequently took over a British General Hospital at Le Treport, France. When this unit was activated and sailed for France on May 18, 1917, Dr. Gibbon was with it as Chief of Surgical Services. In October, 1917, he served on detached duty as surgeon in charge of a Casualty Clearing Station Team in a hospital situated a little above Poperinghe, a small corner of Belgium still held by the Allies.

Shortly after his return to Base Hospital 10, in December, 1917, he was permanently detached from the Pennsylvania Hospital unit and assigned as Consultant in Surgery to the American Expeditionary Forces. He served in the Toul Sector as consultant to the First, Twenty-sixth and Eighty-second Divisions and later to the Fourth Corps. In August, 1918, he was assigned as Surgical Consultant to the American Hospitals in England. He terminated his military service in January, 1919, with the rank of Colonel.

Dr. Gibbon was a past president of the American Surgical Association and the Philadelphia Academy of Surgery as well as the College of Physicians of Philadelphia. He was an original member of the Society of Clinical Surgery.

Dr. Gibbon was the author of sixty or more articles covering a wide range of surgical subjects and several articles historical or philosophical in nature. In 1902, he reported the fourth successful case of penetrating wound of the heart operated upon in this country. In 1903, he reported a case of painless amputation of the leg after the intraneural injection of cocaine. He was quick to seize that which appeared to be good in the newer surgery in an era of rapid surgical progress. He early became interested in aneurisms and wrote a number of papers on the subject. His last listed contribution to the literature, the Presidential Address of the American Surgical Association in 1926, was on "The Psychology of the Sick Man."

Dr. Gibbon was not only interested in the Art and Science of Medicine but in the Humanities as related to the practice of medicine. As an older and more experienced man he never forgot his obligations to the younger generation coming on and was the source of inspiration to all who came within the sphere of his influence. His attitude toward his fellow man was one of kindness and consideration

regardless of station in life. Dr. Gibbon radiated cheerfulness and always seemed to make his patients feel better by his mere presence.

In addition to clinics at Jefferson Hospital, Dr. Gibbon gave a weekly clinic at the Pennsylvania Hospital. Several times a year he presented fractures. These clinics were well known and the amphitheatre at the Pennsylvania Hospital invariably was filled with students from the medical schools of Philadelphia. His lectures were clear and he had the ability to drive home facts.

Beside the many papers published, Dr. Gibbon for a number of years edited the Saunders "Year Book of Surgery" with Dr. John Chalmers Da Costa. He wrote the section on "Compression of Arteries" in Buck's "Reference Handbook of the Medical Sciences" and contributed to the section on "Operative Techniques" in Keen's Surgery.

In 1948, Jefferson Medical College conferred the Honorary Degree of Doctor of Science on Dr. Gibbon because of his significant contributions to Humanity, his Country and the Medical Profession.

Dr. Gibbon suffered a coronary artery occlusion in 1935 while in Boston for a meeting of the American Surgical Association. There he was attended by Dr. Paul Dudley White. He had a second coronary occlusion a few years later and a third early in December of 1955. Despite coronary artery disease he led a happy and interested life and was never inactive for long periods of time.

Dr. Gibbon resigned from teaching positions at the age of 60 chiefly because of a firm belief he had held since early in his career, that older men should not wait too long before making way for younger men. He continued with the private practice of surgery for a few years longer.

After retirement he devoted a great deal of time to carpentry and became a skilled craftsman. He was an avid reader and retained a keen interest in national and world affairs.

On March 13, 1956, he developed pulmonary edema which was sudden in onset. He soon lapsed into unconsciousness and died within a few hours.

Dr. Gibbon's wife lived only seven days after his death. Surviving are a daughter, Mrs. Winthrop H. Battles of Media, three sons, Dr. John H. Gibbon, Jr., Samuel D. Gross Professor of Surgery and Head of the Department of Surgery, The Jefferson Medical College, Samuel Y., of Jenkintown, and Robert, of Haverford, nine grandchildren and three great-grandchildren.

Memoir of Stephen E. Tracy (1875–1956)*

By PHILIP F. WILLIAMS, M.D.

DR. STEPHEN E. TRACY was born in Woodstock, New Brunswick, Canada, on August 27, 1875, the son of George E. and Mary J. Jameson Tracy. His family—of Scottish origin—had lived in New Brunswick for several generations.

After education in the schools of his native Province, Dr. Tracy was graduated from the University of Pennsylvania School of Medicine in 1898. His internship at St. Luke's Hospital, Bethlehem, Pennsylvania, was followed by a residency in the Kensington Hospital for Women in Philadelphia. He joined the staff of the Stetson Hospital upon entering practice, and soon was made co-chief with the late Dr. Charles P. Noble, under whom he had served at Kensington. Dr. Tracy was connected with the Stetson Hospital during his entire professional career, serving as Medical Director for twenty-five years. He was gynecologist to the American Oncologic Hospital, and consultant to the Jewish Maternity and to Mt. Sinai Hospitals in Philadelphia.

Dr. Tracy was a Fellow of the College of Physicians of Philadelphia, of the American College of Surgeons, the American Association of Obstetricians and Gynecologists, and the Obstetrical Society of Philadelphia, (of which he was a past-president). He was a member of the Philadelphia County, and Pennsylvania State Medical Societies. He was certified as a specialist by the American Board of Obstetrics and Gynecology. He served his adopted country in World War I.

Many of us remember Dr. Tracy as a dynamic type of person with an apparently inexhaustible supply of energy. He was one of the guiding spirits in the affairs of the Philadelphia Medical Alumni of the University of Pennsylvania, and for many years effectively directed their winter smokers and the spring picnics. As Chairman of the Publication Committee of the Obstetrical Society he engaged in battle for years with the editor of a certain Journal of Obstetrics and Gynecology regarding the suitability for publication of papers read before the society. He frequently regaled the Society by reading this correspondence.

His early contributions reflect the influence of his preceptors, Estes and Noble, as well as the changing technics and attitudes of the early part of the century. He was regarded as a meticulously careful operator; it is said that he never had recourse to a blood transfusion during operation. His regard for correctness in detail occasionally led him, when operating in an outside hospital to deliver an extemporaneous lecture on errors he noted in the surgical suite.

Dr. Tracy was a conservative surgeon. He consistently tried to conserve ovarian tissue and he advocated myomectomies when feasible rather than excision of the uterus. With an associate he reported one thousand consecutive deliveries with no Caesarean sections. At the Oncologic Hospital, in conjunction with Dr. W. S. Newcomet, he was interested in developing more suitable methods of applying radium in therapy of pelvic malignancy. In this work he constantly stressed the importance of protecting the normal adjacent structures.

Aside from his medical activities, Dr. Tracy was a member of the Union League of Philadelphia, the Medical Club, the Skytop Club, Kiwanis and Old York Road Country Club.

Dr. Tracy died February 22, 1956. His wife, the former Margaret Ann Weaver, predeceased him. He is survived by a son, Stephen, Jr., and a daughter, Mrs. Margaret Mary Witteman.

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

25 February 1957

WOLFF-PARKINSON-WHITE SYNDROME. Michael M. Etzl, M.D., and Charles J. Schreader, M.D. (Discusser: William G. Leaman, Jr., M.D.) (*Abstract 1, below*)

INTERMITTENT CLAUDICATION: PROBLEMS ARISING IN EVALUATION OF TREATMENT. Raymond Penneys, M.D., and Orville Horwitz, M.D. (Discusser: Meyer Naide, M.D.) (*Abstract 2, below*)

USE OF RADIOACTIVE FAT IN THE STUDY OF ABSORPTION IN VARIOUS DISEASE STATES. Donald Berkowitz, M.D., and David Sklaroff, M.D. (Discusser: C. Wilmer Wirts, M.D.) (*Abstract 3, below*)

25 March 1957

INTENSIVE ANTICOAGULANT THERAPY IN THE MORE DANGEROUS CASES OF THROMBOEMBOLISM. Meyer Naide, M.D. (Discusser: William G. Leaman, Jr., M.D.) (*Abstract 4, below*)

EFFECT OF A POLYSORBATE 80-CHOLINE-INOSITOL COMPLEX ON HYPERCHOLESTEREMIA. Charles Bordin, M.D. (Discusser: Daniel A. Sherber,* M.D.) (*Abstract 5, below*)

"PURE ALDOSTERONISM". Joseph M. Gambescia, M.D., Daniel Marino,* M.D., Frank Tropea, M.D., and Joseph Imbriglia, M.D. (Discusser: Walter R. Eberlin, M.D.) (*Abstract 6, below*)

URIC ACID LEVELS IN PERIPHERAL VASCULAR DISORDERS. David W. Kramer, M.D., Paul K. Perilstein,* M.D., and Algy de Medeiros,* M.D. (Discusser: Samuel Lisker, M.D.) (*Abstract 7, below*)

22 April 1957

PATHOGENESIS OF INTERSTITIAL CALCINOSIS. F. William Sunderman,* M.D., and F. William Sunderman, M.D., PH.D. (Discusser: Edward Rose, M.D.) (*Abstract 8, below*)

Q FEVER IN PHILADELPHIA: REVIEW AND CASE REPORT. Fred B. Rogers, M.D., and Robert L. Overman,* M.D. (Discusser: O. Henry Janton, M.D.) (*Abstract 9, below*)

INTERSTITIAL PULMONARY FIBROSIS (HAMMAN-RICH SYNDROME) IN AN ALLERGIC PATIENT: CASE REPORT. Louis Tuft, M.D., and Leonard S. Girsh,* M.D. (Discusser: Thomas M. Durant, M.D.) (*Abstract 10, below*)

THE SERUM PATTERN OF THYROID HORMONES IN STATES OF THYROID DYSFUNCTION. WALTER L. ARONS, M.D. (Discusser: Norman Schneeburg, M.D.) (*Abstract 11, below*)

27 May 1957

QUANTITATION OF MANIFESTATIONS OF RHEUMATOID ARTHRITIS. John Lansbury, M.D. (Discusser: Ralph A. Jessar,* M.D.) (*Abstract 12, below*)

THE SODIUM AMYTAL SEDATION TEST AS A SCREENING PROCEDURE IN THE SELECTION OF DRUG THERAPY IN ESSENTIAL HYPERTENSION. Richard J. Eberly,* M.D., Jerome M. Waldron, M.D., and Garfield G. Duncan, M.D. (Discusser: William A. Jeffers, M.D.) (*Abstract 13, below*)

HOSPITAL INFECTIONS DUE TO ANTIBIOTIC RESISTANT STAPHYLOCOCCI: BACTERIOLOGICAL AND CLINICAL EXPERIENCES AND METHODS OF CONTROL. Norman Learner, M.D., H. Taylor Caswell, M.D., Kenneth M. Schreck,* M.D., Howard H. Steel, M.D., R. Robert Tyson,* M.D., Elsie R. Carrington,* M.D., and William C. Wright,* M.D. (Discusser: Robert I. Wise,* M.D.) (*Abstract 14, below*)

SECTION ON MEDICAL HISTORY

12 February 1957

THE EDWARD BELL KRUMBHAAR AWARD IN MEDICAL HISTORY. Stanley P. Reimann, M.D. (*Transactions & Studies*, June, 1957)

* By invitation.

Edward Bell Krumbhaar: Medical Historian, Bibliophile and Humanist. Samuel X Radbill, M.D. (*Transactions & Studies*, June, 1957)

Oration on the Birthday of Medical Honors in America, by John Lawrence, 1768. Herbert J. Dietrich, Jr., M.D. (*Transactions & Studies*, June, 1957)

John Redman (1722–1808): Medical Preceptor of Philadelphia. Whitfield J. Bell, Jr.,* PH.D. (*Transactions & Studies*, August, 1957)

9 April 1957

The Changing Scene in Harley Street. R. Scott Stevenson, M.D. F.R.C.S. Ed. (Kate Hurd Mead Class of 1888 Lecture in Medical History, Woman's Medical College of Pennsylvania). (*Transactions & Studies*, August, 1957)

SECTION ON OPHTHALMOLOGY[1]

17 January 1957

(Joint Meeting with the Eye Section, Philadelphia County Medical Society)

The Pupil: Theoretical and Practical Considerations. Michael Curcio,* M.D.

Mandibulo-Facial Dystosis. Leonard Apt,* M.D.

Comparative, Experimental and Clinical Studies Using a New Local Anesthetic Agent—Primacaine Hydrochloride. Harold G. Scheie, M.D., and N. S. Williams,* M.D.

7 February 1957

Review of Ocular Virus Diseases. James H. Allen,* M.D.

21 March 1957

(Joint Meeting with the Eye Section, Philadelphia County Medical Society)

Traumatic Hyphemia. Gaylord W. Ojers,* M.D.

Bilateral Sixth Nerve Paresis Simulating Divergence Paralysis—Surgical Correction. E. Howard Bedrossian, M.D.

Temporal Arteritis. Paul Davidson,* M.D., Nathan S. Schlezinger, M.D., and Carroll R. Mullen, M.D.

18 April 1957

Incisions in Cataract Surgery. John M. McLean,* M.D.

SECTION ON OTOLARYNGOLOGY[2]

16 January 1957

An Approach to Diagnosis and Treatment Planning for the Cleft Lip and/or the Cleft Palate Patient. Herbert K. Cooper,* D.D.S.

The Function of an Otolaryngologist in a Cleft Palate Clinic. Lloyd S. Hutchison,* M.D. (Discussers: Robert H. Ivy, M.D., and Oscar V. Batson, M.D.)

20 March 1957

(Joint Meeting with the Section on Otolaryngology of the New York Academy of Medicine in New York City)

Hearing Problems in Children Originating from Lesions Central to the Cochlea. John E. Bordley,* M.D. (Discusser: Douglas Macfarlan, M.D.)

Some Observations on Laryngeal Stenosis. Edwin N. Broyles,* M.D. (Discusser: Chevalier L. Jackson, M.D.)

A New Operation to Restore Hearing in Conductive Deafness of Chronic Suppurative Origin. J. H. Thomas Rambo,* M.D.

11 April 1957

(Joint Meeting with the Philadelphia Laryngological Society)

The Development of Surgery of the Temporal Bone. R. Scott Stevenson,* M.D., F.R.C.S. Ed.

[1] Abstracts of presentations at this Section customarily appear in the *American Journal of Ophthalmology* and the *A.M.A. Archives of Ophthalmology*.

[2] Abstracts of presentations at this Section customarily appear in the *A.M.A. Archives of Otolaryngology*.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

13 February 1957

SEMINAR ON EPIDEMIOLOGY OF CARDIOVASCULAR DISEASES.
Moderator: Robert V. Cohen, M.D.
Guest speaker: Ancel Keys,* PH.D.

20 February 1957

SEMINAR ON EARLY DETECTION AND PREVENTION OF HEART DISEASE, WITH SPECIAL EMPHASIS ON CORONARY ARTERY DISEASE.
Moderator: Robert V. Cohen, M.D.
Guest speaker: David D. Rutstein,* M.D.

5 March 1957

(Joint Meeting with Pennsylvania Public Health Association, Region One) (Arthur Parker Hitchens Lecture II)

PUBLIC HEALTH IN PENNSYLVANIA: HEALTH DEPARTMENT, PLANS AND PROGRAMS. J. Thomas Millington,* M.D., M.P.H. (*Transactions & Studies*, August, 1957)

CANCER AS A PUBLIC HEALTH PROBLEM. Lewis C. Scheffey, M.D. (*Transactions & Studies*, August, 1957)

PROGRESS IN PUBLIC HEALTH IN PHILADELPHIA James P. Dixon, M.D. (*Transactions & Studies*, August, 1957)

ABSTRACTS

Abstract 1

WOLFF-PARKINSON-WHITE SYNDROME. Michael M. Etzl, M.D., and Charles J. Schreader M.D.

The Wolff-Parkinson-White Syndrome or pre-excitation syndrome is a characteristic electrocardiographic pattern occurring in 0.2% of electrocardiograms taken in a general hospital. This syndrome is usually devoid of clinical manifestations, unless associated with paroxysms of tachycardia which occurs in approximately 70% of patients.

The characteristic features of the electrocardiogram are a PR interval of 0.10 seconds or less and a QRS duration of more than 0.10 seconds. In 15% of cases the PR interval may be 0.12 seconds or longer. The lengthened QRS compensates for the shortened PR interval and the PJ cycle remains constant, measuring 0.26 seconds or less. The initial ventricular activation is usually slurred and is termed the delta wave. The extent of slurring or height of the delta wave is dependent on the speed of normal atrio-ventricular conduction. The onset of ventricular activation, through the normal conduction pathway, vitiates the activity of the accessory pathway and is graphically indicated by the end of the delta wave. ST segment and T wave aberrations are usually opposite the main deflection.

Some sixty theories have been advanced to clarify this mechanism. Two prominent theories may be worthy of mention. The theory of "accelerated conduction through the normal pathway" proposed by Prinzmetal embodies the concept that the A-V node does not act as a whole—part conducts at an accelerated rate, while the other part maintains its normal rate of conduction. The Accessory Pathway or Bundle of Kent theory implies one or more accessory pathways which may by-pass the normal A-V delay. We feel that it is congenital anomaly which may be anatomically present but physiologically dormant. Disease, mechanical, or drug depressant action may alter normal conduction and allow the accessory bundle to become manifest. The majority of the arrhythmias are supraventricular tachycardias, auricular flutter or auricular fibrillation. Ventricular tachycardia may be simulated by a supraventricular tachycardia with aberrant conduction.

Electrocardiograms were shown to demonstrate examples of right and left accessory bundles. The classical response to carotid sinus pressure, amyl nitrite and digitalis in producing the W.P.W. pattern and its disappearance with quinidine, was demonstrated. Interesting E.C.G. tracings of typical W.P.W. pattern progressing into an atrial tachycardia with aberrant ventricular conduction simulating ventricular tachycardia were also shown. Its supraventricular origin was proven by

displaying the presence of auricular flutter converting to auricular fibrillation.

An unusual tracing of atrial tachycardia with alternation of pre-excitation pattern following cedilanid was shown. Exceptional instances of prolonged PR interval of 0.15 seconds and PJ cycle of 0.30 seconds were also shown.

The clinical importance of recognizing this syndrome, to prevent confusion with intraventricular conduction defects, supraventricular tachycardias occurring with or without associated organic heart disease, was discussed. From our studies we feel justified in favoring the existence of a congenital anomalous pathway as the feasible explanation for the pre-excitation syndrome.

Abstract 2

INTERMITTENT CLAUDICATION: PROBLEMS ARISING IN EVALUATION OF TREATMENT. Raymond Penneys, M.D., and Orville Horwitz, M.D.

Studies were made on 51 patients having intermittent claudication of the lower extremities resulting from arteriosclerosis obliterans. Observations on these patients, who received no specific treatment for their claudication, show that claudication (1) may remain of only symptomatic importance (these patients had had their claudication for an average of 68 months at the time of this writing, without loss of limb or livelihood); (2) often appears to improve with time alone (in a two-year follow up on 38 patients, they stated that their walking distance had increased from an average of 1½ city blocks to an average of 3½ blocks); (3) is often present in both legs (29 patients); (4) varies considerably, even in the same patient on the same day, when measured on a treadmill; (5) is often associated with coronary artery disease (18 patients).

These features of intermittent claudication must be appreciated before the value of any treatment for claudication can be properly assessed.

Abstract 3

USE OF RADIOACTIVE FAT IN THE STUDY OF ABSORPTION IN VARIOUS DISEASE STATES. Donald Berkowitz, M.D., and David Sklaroff, M.D.

The recent availability of radioactive labeled fat has made it possible to study fat absorption with a minimum amount of technical difficulty. The procedure used consists of giving a test meal containing triolein labeled with I^{131}. The radioactivity of serial blood samples is then determined and may be expressed as the percentage of fat ingested. This method gives reproducible results and correlates well with more elaborate chemical balance studies.

Twenty five normal controls and seventy-five patients with various diseases have been studied, and the results in these will be discussed. In pancreatic or small bowel disease, varying degrees of impairment of fat absorption are found. On the other hand, patients with liver disease, in general show no abnormality. Preliminary studies in a group of jaundiced subjects indicate that this test may be of differential diagnostic value in determining the type of jaundice.

The isotopic fat technique would thus appear to provide another approach to the study of small intestinal absorption, which is at present poorly understood.

Abstract 4

INTENSIVE ANTICOAGULANT THERAPY IN THE MORE DANGEROUS CASES OF THROMBOEMBOLISM. Meyer Naide, M.D.

In most patients with venous and arterial thrombosis and embolism the routine methods of using heparin and dicoumarol are adequate. In the routine method heparin and dicoumarol are started and then when the prothrombin is at an effective level heparin is stopped, usually within two or three days. However, in using heparin and dicoumarol in this manner the most dangerous types of patients, particularly those with pulmonary emboli from venous thrombi and patients with arterial emboli,

may not be receiving effective anticoagulant therapy.

During the past three years the use of a more intensive program of anticoagulant treatment with heparin and dicoumarol has proven of considerable value in managing this dangerous group of patients. The program consists of the use of heparin throughout the entire period in which dicoumarol is used, two or three weeks or longer. The heparin is administered intravenously at first and then intramuscularly. The use of two anticoagulants, heparin and dicoumarol, straight through the period of treatment, may be life-saving in some patients by preventing embolism during the escape of the prothrombin out of an effective level by the concomitant constant administration of heparin. Furthermore, the use of these two anticoagulants throughout the period of danger has prevented fatalities even when pulmonary emboli have occurred during the course of treatment because the clot did not become large enough to be fatal. Using heparin and dicoumarol in this manner has been effective in the avoidance of vena caval or iliac vein ligations in a good many of the treated patients—but not in all.

Abstract 5

EFFECT OF A POLYSORBATE 80-CHOLINE-INOSITOL COMPLEX ON HYPERCHOLESTEREMIA. Charles Bordin, M.D.

The evidence linking prolonged hypercholesteremia with atherosclerosis is discussed, and in view of this evidence it would appear that sustained reduction of excessive blood cholesterol is desirable.

Blood cholesterol levels were determined in 39 well controlled diabetics and 17 were found to have hypercholesteremia (over 300 mg./100 cc). The atherosclerotic retinal, peripheral vascular and cardiovascular complications in these hypercholesteremic patients were then determined by means of eye and peripheral vascular examinations and by electrocardiography. Evidence of atherosclerosis was found in 13 of the 14 patients studied. By comparison, only 4 of the 7 patients in the "normocholesteremic" group who had such studies presented evidence of atherosclerosis.

The effect of administration of a polysorbate 80-choline-inositol complex (Monichol) on the elevated blood cholesterol levels was investigated in 14 of these hypercholesteremic diabetics. The treated patients were instructed to take one teaspoonful (5cc) of the medication four times daily, for a period of two to five months. There were no significant changes in insulin dosage, diet, weight and degree of diabetic control during this period. Significant reductions in cholesterol levels occurred in 13 cases. After medication was stopped for an average period of three months, serum cholesterol levels were again determined in the 14 treated patients. In every case the cholesterol levels returned to their pre-treatment values. Of the hypercholesteremic diabetics showing evidence of atherosclerotic complications, some improvement was observed in 2 patients in this short term study.

The probable mechanism of action of the polysorbate 80-choline-inositol complex is by an alteration of the physical state of the cholesterol molecule, increasing its filtration through the renal glomeruli, and enhancing its utilization by the adrenal cortex. The treatment regimen will be continued to determine whether prolonged use of the complex and correction of hypercholesteremia will be of benefit to the diabetics with atherosclerotic complications.

Abstract 6

"PURE ALDOSTERONISM." Joseph M. Gambescia, M.D., Daniel Marino, M.D., Frank Tropea, M.D., and Joseph Imbriglia, M.D.

Conn's 'Primary Aldosteronism' is classically hypertension without edema, polyuria, polydypsia, weakness and "paralysis". This accompanies a hyperchloremic alkalosis associated with hypokalemia and hypernatremia. This may be due to adrenal cortical adenoma, adrenal cortical hyperplasia, or adrenal carcinoma with increased output of aldosterone in the urine.

The case presented revealed some of these characteristics, viz., polyuria, polydypsia, weakness, and no edema associated with hypokalemia; also hypernatremia but no hypertension and no hypokalemic alkalosis, but increased amounts of aldosterone in the urine.

Operation revealed adrenal hyperplasia and subtotal adrenalectomy was accompanied by recovery from the metabolic disturbances.

It is postulated that this manifestation of 'Primary Aldosteronism' may be the effect of only the biologic activity of aldosterone and that the hypertension and hypokalemic alkalosis may be due to secretion of 11 and 17-oxysteroids. Hence the picture of 'Primary Aldosteronism' may be due to secretion by the adrenal cortex of excessive amounts of 11 and 17-oxysteroids as well as aldosterone—a mixed tumor. The case presented might also be an early stage of the overt clinical picture.

Abstract 7

Uric Acid Levels in Peripheral Vascular Disorders. David W. Kramer, M.D., Paul K. Perilstein, M.D., and Algy de Medeiros, M.D.

High uric acid levels may be found in a variety of conditions, particularly in gout. Gouty individuals are, presumably, more liable to develop arteriosclerotic changes, but no definite study has been made upon its possible influence in arterial diseases.

A survey of uric acid determinations was made in 351 patients with various vascular disorders, including artery and vein conditions. Serum uric acid levels from 2–6 mg. were adopted as normal.

Among the arterial cases, 20.3% showed hyperuricemia. The highest percentage was in the abdominal aorta conditions, 28.4%; the arteriosclerotic group, 20%; arterial thrombosis, 19.3%; and diabetic atheromatosis, 8.9%. Among 80 patients with thrombophlebitis, 11.3% had hyperuricemia.

A study of the levels according to the severity revealed that 24 cases (28.2%) of the severe types had a uric acid level above 6 mg.; 21 cases (18.1%) of the moderate group, and 8 cases (15.5%) of the slight or mild forms. Of the 17 cases who showed calcification, but no evidence of thrombosis, only 2 (11.8%) had hyperuricemia.

An analysis according to sex showed a striking predominance of males over females, 7:1, among those cases where uric acid levels were above 6 mg.%. Among the patients with levels below 6 mg., the ratio dropped to 1.9:1.

From our survey, hyperuricemia could not be considered merely as an incidental finding. The association, particularly with the arterial thrombosis and the higher percentage according to the severity of involvement, suggests that it may play some role, either directly or indirectly in the development of thrombosis.

Abstract 8

Pathogenesis of Interstitial Calcinosis. F. William Sunderman, Jr., M.D. and F. William Sunderman, M.D., PH.D.

Metabolic studies are reported on patients suffering from extensive interstitial calcinosis. A balance study on one of the patients demonstrated negative calcium balance on a restricted calcium diet. The patient ingested an average of 145 mg. of calcium per day and excreted 275 mg. Thirty percent of the excreted calcium was present in the urine and seventy percent appeared in the feces. Since normal individuals ingesting a calcium-restricted diet characteristically develop a similar negative calcium balance, these studies support the view that interstitial calcinosis is *not* associated with disturbance in the normal response to calcium deprivation.

The administration of ammonium chloride in addition to the restricted calcium diet, increased the urinary excretion of calcium seventy percent. Diminution in size and number of calcium deposits following this regimen indicated that the interstitial deposits were not sequestrated but remained in reversible dynamic equilibrium.

Interstitial calcification produced experimentally in guinea pigs by a diet deficient in the anti-stiffness factor (Stigmasterol) bears resemblance to interstitial calcinosis of man.

Especial note is made of the structural similarities of stigmasterol to calciferol (Vitamin D_2). It appears paradoxical that diets deficient in stigmasterol may produce interstitial calcifications, whereas a dietary *excess* of calciferol may likewise yield extra-skeletal calcifications.

The pathogenesis of interstitial calcinosis appears to involve an abnormal affinity of the mucopolysaccharide of extracellular ground substance for calcium. It is noteworthy that interstitial deposits of calcium phosphate are produced without significant alterations in the concentrations of serum calcium or inorganic phosphorus, and without disturbance in the normal pattern of calcium excretion.

Abstract 9

Q Fever in Philadelphia: Review and Case Report. Fred B. Rogers, M.D., and Robert L. Overman, M.D.

Q fever, an acute infectious disease caused by *Coxiella burnetii*, was first recognized by E. H. Derrick in Australia in 1935. A self-limited systemic disease, several epidemics were reported among troops in southern Europe during World War II. In 1946, outbreaks were described in Amarillo, Texas, and Chicago meat-packing houses, and in 1947 Q fever was found to be endemic in California. Since then this disease, important in the diagnosis of non-bacterial pneumonias, has been reported from various parts of the world and appears to have a cosmopolitan distribution.

Today, Q fever is being encountered with increasing frequency in the United States. Furthermore, this highly communicable rickettsial infection may cause severe illness—which may prove fatal in older persons. The actual method of transmission of the disease to man is uncertain. Its spread is largely airborne among individuals in close contact with livestock; wool, hair, hides, offal and raw milk have been incriminated as possible vehicles for transmission through infected ticks to humans. Clinically, Q fever usually produces an interstitial pneumonia. Rickettsemia occurs during the febrile period and specific complement fixing antibodies are present during convalescence. In contrast to other rickettsioses, there is no skin rash and no agglutinins for the proteus bacteria (negative Weil-Felix reaction).

While numerous cases have been described in the western United States, few have been seen east of the Mississippi River. In 1949, Janton et al. reported the first case of naturally acquired Q fever in the eastern United States—a 36 year old white man who worked in a wool-processing factory at Philadelphia. Our patient is the second serologically-diagnosed case of this disease in Philadelphia.

This 42 year old Negro man was admitted to Temple University Hospital on January 28, 1957, complaining of fever, malaise, weakness, cough and left-sided chest pain—of one week's duration. He continued working in a burlap mill until the day before hospitalization. This mill used fiber and rags from various sources for burlap manufacture. One supplier of cloth remnants was a nearby fertilizer plant which used blood and bone meal from animal sources. The patient's past history included mild respiratory infections in 1951–52, and moderate alcoholism.

Physical examination showed a robust Negro man—febrile (104°) and restless. Bronchovesicular breath sounds, whispered pectoriloquy and a soft pleural friction sound were auscultated over the left lower, anterior chest. A relative bradycardia (96 per minute) coexisted. The spleen was not enlarged and there was no skin rash. Laboratory studies: slight polymorphonuclear leukocytosis and elevated sedimentation rate. Serologic tests for syphilis non-reactive. Chest x-ray detected a patchy, confluent abnormal density in the lingula and posterior portions of the left upper lobe—with prominence of the interlobar septum and obscuration of the left heart border. Electrocardiogram was normal. Skin test for tuberculosis (P.P.D. ⅜ 1) was negative. Cold agglutinins, adenovirus and influenza A and B virus studies were negative. Serial complement fixation tests for *Coxiella burnetii* antibodies were compatible with a diagnosis of Q fever—less than 1:8 on 1/29/57, 1:16 on 1/31/57, and 1:256 on 2/5/57.

The patient was given penicillin and streptomycin for two weeks without appreciable improvement. Tetracycline was substituted during the last two weeks of hospitalization. During his hospital stay, his fever and pneumonia gradually subsided. He was discharged on February 27, 1957—recovered. The diagnosis of Q fever was reported to the Philadelphia Health Department as required. An epidemiologic investigation was conducted by health officials to detect possible sources of infection or other cases of the disease, but none was found.

Abstract 10

INTERSTITIAL PULMONARY FIBROSIS (HAMMAN-RICH SYNDROME) IN AN ALLERGIC PATIENT: CASE REPORT. Louis Tuft, M.D., and Leonard S. Girsh, M.D.

The case being reported is one of diffuse interstitial pulmonary fibrosis diagnosed antemortem by lung biopsy and successfully treated with long-term cortisone therapy. This condition was first described in 1935 by Hamman and Rich as a fatal pulmonary disease of unknown etiology and is now known as the "Hamman-Rich Syndrome." Since then, a total of 40 cases of this disease has been collected. Originally, the diagnosis was established postmortem after careful microscopic studies. But in three more recent cases, including the present one, diagnosis was made antemortem by lung biopsy. This permitted earlier institution of treatment and in two cases more favorable therapeutic response. Thus, the patient reported by Pinney and Harris in February 1956, has remained clinically well after 17 months of cortisone therapy and thus far our patient is still living after 14 months of prednisone therapy.

Our patient, a 44 year old white woman, was first seen November 8, 1955, because of cough, increasing dyspnea and fatigue. Her general health always was good except for recurrent attacks of nasal difficulties diagnosed as "sinusitis" for about 15 years, especially in the spring and more recently in the fall. She also had several bouts of hives induced by eating strawberries or pork. The family history was strongly positive for allergy.

Her present illness began about May 1953, when she noticed increasing fatigue, irregular menses and weight loss for which she took an estrogenic hormone (Sulestrex) for more than a year without benefit.

In June 1954, she was treated for so-called viral pneumonia. Treatment with aureomycin was followed by severe diarrhea of one week duration. A chest x-ray revealed a diffuse mottling, considered part of the pneumonic process. Her symptoms persisted and she was admitted to Lancaster (Pa.) General Hospital in October, 1954. Chest x-ray again showed nodular extradensities reported as suggesting either asbestosis or Boeck's sarcoid.

She obtained slight symptomatic relief from ambodryl; but in May 1955, she had another viral penumonia-like episode. Following this, she continued to have pain in the right upper chest, increasing dyspnea, fatigue, and weight loss, and was hospitalized at Temple University Hospital on January 3, 1956. Examination showed slight fever, clubbing and cyanosis of the fingers and increased breath sounds and rales in the upper chest posteriorly. Chest x-ray showed increase in the diffuse mottling throughout the lungs suggesting Boeck's sarcoid, reticulo-endotheliosis, or the Hamman-Rich Syndrome. All laboratory examinations were negative except for a 6% eosinophil count, and positive allergy tests to house dust, tobacco, and ragweed pollen. The patient was so exquisitely sensitive to tobacco smoke that the inhalation of even the slightest amount induced cough and dyspnea. Arterial oxygen saturation was 69% with only slight impairment in ventilatory function. Histological examination of a lung biopsy specimen removed by open incision on January 12, 1956, showed pathological changes compatible with the Hamman-Rich Syndrome. No evidence of beryllium deposit was found in these sections.

The patient's condition worsened and she was again hospitalized on February 20, 1956 with evidence of cardiac failure. She first was digitalized and then given prednisone 5 mg.

four times daily. This has been continued to the present time with striking improvement in her appetite and well being and progressive weight gain. She has no dyspnea except on excessive exertion, her arterial oxygen saturation now is practically normal (94%), and a recent comparative chest x-ray shows slight but definite lessening in the degree of lung density.

From clinical data and radiological evidence in our patient, the diagnosis of diffuse pulmonary fibrosis, the Hamman-Rich Syndrome, could only be suspected. Definite confirmation was possible only after histological examination of the lung biopsy specimen.

Among possible suggested etiologies are virus infections and drug allergy. That this disease might represent a reaction of drug allergy is indicated by the fact that 14 of the 40 cases reported received potent sensitizing drugs prior to the onset. This could not be substantiated in our patient despite her allergic tendencies. However, we later obtained a history from her of continued inhalation of irritating fumes from a nearby factory for about two years prior to the onset of her symptoms. This must be considered as a possible etiologic factor, especially when one is dealing with such a susceptible patient and a disease whose etiology is undetermined.

The favorable response to cortico-steroids in our patient and in that of Pinney and Harris in contrast to their failure in 8 others emphasizes the necessity of their administration as early as possible in the course of the disease and their continuance for an indefinite period; also that their administration should never be discontinued abruptly, if at all.

Abstract 11

THE SERUM PATTERN OF THYROID HORMONES IN STATES OF THYROID DYSFUNCTION. Walter L. Arons, M.D.

Radiopaperchromatographic studies have been carried out following the administration of therapeutic doses of radioactive iodine (I^{131}) on the sera of 25 euthyroid and 25 hyperthyroid subjects and in twelve patients with thyroid cancer. Chromatographic separation of the thyroid hormones was effected in butanol-ammonia and/or tertiary amyl alcohol ammonia solvent systems. Paper chromatograms were then divided into 0.5 cm. horizontal strips for radioactivity measurement in a scintillation well counter. Sera were characterized for the presence of thyroxine, 3:5:3′ triiodothyronine, monoiodotyrosine and diiodotyrosine at varying intervals from one to 144 hours after the administration of I^{131}.

In all cases the major concentration of radioactivity was in the thyroxine area. Triiodothyronine activity was demonstrable in the sera of 9 out of 25 hyperthyroid subjects but only in 2 of 25 euthyroid sera. No definite monoiodotyrosine or diiodotyrosine activity was noted in any of the patients. A functioning thyroid metastasis was shown to be capable of producing both thyroxine and triiodothyronine. The administration of thyroid stimulating hormone (TSH) to 5 euthyroid subjects was followed by a prompt rise in serum radiothyroxine levels alone while the administration of TSH to 4 hyperthyroid subjects was followed within 3 hours by small rapid, but transient increases in serum radiotriiodothyronine levels as well as by rises in thyroxine activity.

The metabolic implications of these data were discussed, particularly with reference to the possible role of the thyroid gland in the acute body response to stress.

Abstract 12

QUANTITATION OF MANIFESTATIONS OF RHEUMATOID ARTHRITIS. John Lansbury, M.D.

In chronic diseases such as diabetes, myxedema, anemia and hypertension, the following observations are an indispensable guide to management: blood and urine sugar determinations, BMR, hemoglobin and blood pressure readings. In rheumatoid arthritis we urgently need a comparable indicator of the severity or activity of the disease process. The systemic and articular indices which are described below are offered as a solution to this pressing problem.

Rheumatoid arthritis provides us with a profusion of observable data. Our task is to

select from among them those items which are universally present in some degree and which can be quantitatively observed and which therefore lend themselves to a simple process of summation so that their average degrees of severity can be expressed in a single figure.

The following items fulfill these criteria:

1. Duration of stiffness after rising in the morning.
2. Length of time after rising before the patient's usual occupation causes fatigue.
3. Number of aspirin tablets required per day to control pain.
4. Strength of the hand grips as measured by an ordinary blood pressure cuff.
5. Sedimentation rate.

These items are summed up into a *Systemic Index* by referring to tables which translate the actual clinical observations into percentage values. The method has the great advantage of requiring only 5 to 10 minutes for collecting the information and another 2 to 3 minutes to make the calculations. In patients proceeding to a remission the values of the Systemic Index decline in a regular manner as the activity of the disease subsides whereas, if the disease is static, the index is unchanged. Our records over a period of over 2 years indicate that the index reflects with great accuracy our clinical impressions of the course of the disease in a large number of patients. We have seldom if ever seen a definite change in the index that did not reflect our own or the patient's opinion as to a change for better or worse.

In the past numerous efforts have been made to evaluate the progress of the disease by means of joint findings, but, without a method for summing them up, it is difficult to use these findings as an index of the patient's status. We present a solution for this difficulty by taking into account the size of the involved joints. This is based on the total area of articulating surfaces of the extremity joints which, in an average sized individual, amounts to about 1 square meter. The Articular Index is derived from a table of joint sizes by writing down the numerical value of each involved joint instead of its name. The values are then added up, their sum, (÷ 10) constitutes the articular index. By this method one can record the simple extent or "spread" of articular involvement, or, if one believes that individual joint findings can be quantitated, one can likewise add up this information too.

We have found that a good correlation ($r=0.78$) exists between the Articular Index and the Systemic Index. Because they measure two quite different things, this strongly suggests that the systemic index is reliable through the full range of activity of the disease process.

Infections with these antibiotic resistant organisms do not constitute a temporary epidemic but represent a problem which must be faced for an indefinite period of time in our modern antibiotic-saturated hospital society. Infected hospital personnel play a dominant role in the transmission of these organisms. The role of the healthy nasal carrier is equivocal. Control of these hospital staphylococci cannot be attained by the discovery of additional antibiotics, for resistance to these new agents will probably develop as it has to the ones previously employed. Successful control must be predicated on a return to strict sterile techniques combined with intelligent limitation of the use of antibiotic agents.

We recommend a trial of this new approach to the quantitation of the disease. In our two year's experience with it, we have found it exceedingly useful in guiding therapy and in making a permanent record of the actual status of each patient.

Abstract 13

THE SODIUM AMYTAL SEDATION TEST AS A SCREENING PROCEDURE IN THE SELECTION OF DRUG THERAPY IN ESSENTIAL HYPERTENSION. Richard J. Eberly, M.D., Jerome M. Waldron, M.D., and Garfield G. Duncan, M.D.

The sodium amytal sedation test was introduced as an aid in the evaluation of patients having essential hypertension and for whom a sympathectomy was being considered. This test was of no consistent value in the selection of patients for this procedure, and the test fell into general disuse. Nevertheless, it re-

mained a part of the evaluation of some hospitalized hypertensive patients. We have reviewed the records of patients in whom the test was employed and have tried to determine whether or not it might be helpful in predicting the probable response of those patients to the newer hypotensive drugs.

The hypotensive drugs now in general use are divided into two groups: those producing ganglionic blockade, and all other agents. From a review of twenty-two sodium amytal tests done in a uniform manner within the past two years at the Pennsylvania Hospital, it was possible to divide the responses of the diastolic blood pressure into three categories: labile, intermediate, and fixed.

Comparing the tabulation of response to sodium amytal sedation with that to hypotensive drugs, it became apparent that, in general, patients whose diastolic pressures are labile, or reduced to 90 mm. Hg. or lower during the test will achieve a good reduction in blood pressure with mild hypotensive drugs. In contrast, those patients whose diastolic blood pressures are fixed, or are not significantly altered during the test generally do poorly on mild drug therapy and require ganglionic blockade if adequate reduction of the blood pressure is to be achieved. In addition, the blood pressure was rarely reduced more with conservative drug therapy than was obtained during sodium amytal sedation. A reasonable prediction of the hypertensive patient's response to various drug therapies is therefore possible by observing the response of the diastolic blood pressure to sodium amytal sedation, on the patients' first evening in the hospital and before hypotensive drugs have been given.

In one patient with hypertension, diabetes, and advanced cardio-vascular-renal changes, the labile response of the diastolic blood pressure to sedation with sodium amytal suggested that the diabetes was the cause of damage to function in these organs, and not hypertensive disease. The amytal test may therefore be helpful in differential diagnosis.

This review of sodium amytal tests suggests a further investigation of this simple and safe hospital study as a guide in the drug therapy of essential hypertension.

Abstract 14

Hospital Infections Due to Antibiotic Resistant Staphylococci: Bacteriological and Clinical Experiences and Methods of Control. Norman Learner, M.D., H. Taylor Caswell, M.D., Kenneth M. Schreck, M.D., Howard H. Steel, M.D., R. Robert Tyson, M.D., Elsie R. Carrington, M.D., and William C. Wright, M.D.

Bateriological and clinical experiences with antibiotic resistant staphylococcal infections at Temple University Medical Center over a period of one year are presented. The current problem of hospital infections with these organisms is world-wide.

Bacteriophage typing revealed that 69% of significant hospital infections were of bateriophage type 42B/52/81. This compares with a 16% incidence of this bacteriophage type in patients admitted with staphylococcal infection. Only 4.1% of 265 nasal carriers of coagulase positive staphylococci among hospital personnel were infested with organisms of this bacteriophage type. Thus, nasal carriers of staphylococci among hospital personnel played an insignificant role in the transmission of the organism in our institution. Efforts for control of hospital infections with Staphylococcus aureus must include measures directed with equal vigor toward both airborne and direct contact routes of transmission.

Novobiocin and chloramphenicol were the only two antibiotics studied by us to which these organisms were highly susceptible. Staphylococci resistant to both of these antibiotics can, and are, developing—as they have developed after the use of the older antibiotics. The use of novobiocin and chloramphenicol and newly introduced antibiotic agents to which staphylococci are susceptible should be limited to those patients with significant staphylococcal infection whose organisms are not susceptible to any other antibiotic or chemotherapeutic agent and whose infection cannot be controlled by other means such as adequate surgical drainage.

College Notes

New Fellows

The following were elected Fellows on the dates listed:

6 February 1957

S. Stanley Barr
Frances Dees-Porch
Richard A. Ellis
Howard Isaacson
Edward L. McConnell, Jr.
Joan Mary Roberts
Joseph W. Spelman
Alexander Witkow

6 March 1957

Louis H. Bloch
Frank L. Cohen
William J. Erdman, II
Michael M. Etzl
Donald S. Frankel
Simon B. Forman
George R. Fornwalt
Leon Kacher
David G. Moyer
Richard S. Oakey, Jr.
Edward P. L. Shope
Nathan Schnall
Robert C. G. Stanley
Jerry Zaslow

3 April 1957

Thomas M. Birdsall
Vincent J. Cattie
A. H. Boyer Drake
Luke W. Jordan
Russell C. Seipel
John R. Wolgamot

8 May 1957

Albert M. Biele
John A. Calhoun
Arthur R. Errion*
Thomas R. Hedges, Jr.
N. William Winkelman, Jr.

* Non-Resident. (Medical Corps, U. S. Navy).

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Current Views on Insulin Action[1]

By WILLIAM C. STADIE, M.D.[2]

THE understanding of the symptoms of a metabolic disease such as diabetes is dependent upon a knowledge of the chemical reactions which underlie biological activity. A requisite for this understanding is a knowledge of the functions of the enzymes and co-enzymes which bring about a series of orderly molecular changes in the available foodstuffs within the cell. Cellular homeostasis can then be discussed in terms of the complex reactions catalyzed by the cellular enzyme systems. When these finely integrated chemical reactions are disturbed, there is a departure from normal metabolic function; the abnormal condition which results is the disease. But enzymatic action is influenced by a great variety of endocrines arising, for example, from the alpha or beta cells of the islands, from the pituitary, adrenals, etc. In diabetes, these considerations generate two separate problems for investigation. The first is the problem of the metabolic defect, that is, the recognition of the nature of the disturbances of the complex interrelations of enzymes, co-enzymes, and hormones which occur in this disease. The second is the problem of the mode of action of insulin; that is, the description of the mechanisms by which insulin eliminates these defects. Thirty-five years have elapsed since the discovery of insulin; nevertheless, these two problems are still obscure and continue to be fields for active experimentation and speculation. I propose to discuss in this paper some experiments designed to illumine these two areas. A pattern begins to reveal itself and I shall undertake to describe this pattern as I see it.

One more remark of a general character needs to be made, I believe, before plunging into the discussion of details of metabolism in diabetes. Study of the diabetic defect and the mode of action of insulin can be approached in two ways. The first is to couch the discussion in terms of specific chemical reactions. For example, we may ask: Is the reaction:

$$\text{Glucose} + \text{phosphate} = \text{glucose-6-phosphate}$$

that is, the hexokinase reaction, impaired in the diabetic state? Or: Does insulin accelerate the reaction:

$$2 \text{ acetyl Co-A} = \text{butyryl Co-A}$$

a reaction necessary for the synthesis of higher fatty acids? Indeed, our knowledge of the metabolic aspects of diabetes is almost exclusively composed of the answers to innumerable questions of a similar character.

[1] Alvarenga Prize Lecture XVII, College of Physicians of Philadelphia, 2 October 1957.

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The second approach is to direct our speculations toward possible alterations of molecular configurations of tissue catalysts: For example, we may ask: Is insulin a part of an enzyme system so that the substrate "fit" is improved and catalysis of this metabolite is accelerated? Or: Does insulin become part of an electron chain so that an assumed impediment in electron flow is removed and therefore oxidation of some substrate is increased? This field of "molecular medicine" has scarcely been touched. Linus Pauling has made the initial explorations in his description of the molecular changes in hemoglobin occurring in sickle cell disease and other abnormal hemoglobin syndromes. Pauling (1) also speculated about the possible therapeutic elimination of the enzymatic defect which is at the basis of phenylpyruvic oligophrenia. In the problem of the action of insulin, the only demonstration with which I am familiar of what might be called a molecular phenomenon is the demonstration in our laboratory (2) that insulin is bound by tissues. In the rat diaphragm, the reaction is very rapid and the bound insulin exhibits all of its characteristic properties.

A short discussion of this phenomenon is appropriate here. The introduction of insulin labeled with radioactive iodine made it possible to measure with accuracy the minute amounts of insulin bound to tissue. It was shown, for example, that the increased glycogen synthesis from glucose by the isolated rat diaphragm was proportional to the amount of insulin bound to the tissue. Thus for the first time the response of a tissue to a known amount of hormone is accelerating a specific chemical reaction was measured. Almost all the tissues of the body bind insulin but in different concentrations. The amount bound by muscle or liver tissues with high rates of metabolism is high. The binding capacities of the structural elements of the liver, i.e. mitochondria, nuclear fraction, and microsomes, are different indicating a specificity of the binding. The brain, which has never been shown to react to insulin, shows no bound insulin following intravenous injection of the hormone in the intact animal. This organ, then, appears to have a metabolism not requiring insulin.

In the case of the rat diaphragm studied *in vitro*, the behavior of the bound insulin is in complete accord with our knowledge of its action obtained in other ways. The response to bound insulin is diminished in the alloxanized animal. It is also diminished by the injection of cortisone and growth hormone which are known to be insulin antagonists. In the hypophysectomized rat, amounts of bound insulin which in the normal rat are without effect upon glucose uptake, have almost maximum effects. This is in accord with the well known insulin sensitivity of the hypophysectomized animal. Adipose tissue and lactating mammary gland also respond to bound insulin. The binding of insulin by tissues may have analogous implications to the binding of substrates by enzyme systems. For example, Stetten has attempted to calculate for insulin-tissue binding a constant similar to the Michaelis-Menten constant for enzyme-substrate binding. However, the full significance of the phenomenon remains to be worked out.

These concepts of the metabolic effects of insulin are necessarily complex but inevitably yield practical benefits. One recent practical benefit which has come out of the knowledge of the action of insulin which has accumulated in the literature during the past quarter century is the evaluation of the therapeutic usefulness of the hypoglycemic drugs which have been recently introduced in the treatment of diabetes. The experimenter had available patterns of behavior of the metabolism of the mammalian organism in response to the administration of insulin. With this knowledge, experimental designs could be formulated for testing the action of the oral hypoglycemic drugs. Thus, within a relatively short space of time it was shown that the responses of mammalian metabolism to the drugs were quite different from those of insulin. They were, therefore,

not insulin substitutes but accessory agents which could be used with benefit in a limited number of cases.

Turning now to the discussion of metabolism in diabetes, I shall discuss two hypotheses which have been formulated to explain why the early steps in the dissimilation of glucose are impaired in diabetes. The first metabolic reaction of glucose is a reaction with inorganic phosphate to form glucose-6-phosphate catalyzed by the enzyme hexokinase. This phosphorylation of glucose is a pre-requisite for its further metabolism. Impairment of this reaction would necessarily bring to a halt all further metabolic reactions of the sugar. Experiments reporting inhibition of the hexokinase reaction in extracts of the muscles of diabetic animals have been reported, but these findings have not been confirmed. So far as muscle is concerned, it is now generally held that impairment of the hexokinase reaction does not play any role in the decreased ability of the muscle to metabolize glucose. However, this conclusion does not necessarily hold for the liver, and the possibility still remains in the diabetic animal that a defect of glucose metabolism in that organ might be due to deficient glucose-6-phosphate formation owing to an inhibition of hepatic hexokinase.

A second hypothesis concerning insulin action in muscle involves the role of the cell membrane in early glucose metabolism. This was first suggested by Hoeber (3) in 1927, who proposed a "membrane theory of diabetes." He said: "One thinks that an abnormal constitution of the cell membrane does not allow the simple sugars to reach their normal locus of breakdown. If one considers the above possibility we may substitute for the present theory of diabetes, which is based upon concepts of abnormal enzymatic activities, another theory, namely the membrane theory of diabetes." Hoeber himself presented no experimental data to support this hypothesis and some 25 years passed before two investigators, Levine (4) of Chicago and Ross (5, 6, 7) of London, studied the possible role of permeability factors in diabetes, each approaching the subject from different points of view.

Levine's experimental design was simple in principle. First, he used the completely eviscerated dog. Second, he selected sugars, for example, galactose, which are not metabolized by these eviscerated animals. Using this experimental system he calculated from the constant levels of blood sugar established, the volume of distribution of sugars following intravenous injection. He found, for example, in the case of galactose, that in the absence of injected insulin, the blood galactose level established, indicated a volume of distribution of 45% of the body weight, approximately that of the extracellular space. In the same preparation, when insulin was simultaneously injected with the galactose, the volume of distribution was 70% of the body weight, essentially that of body water. Levine concluded from these data that in the absence of insulin the galactose was practically excluded from the muscle cell. Following insulin injection the barrier which had excluded the sugar from the cell was eliminated; the galactose then distributed itself throughout the whole of body water. In similar experiments Levine studied other sugars and he divided them into two groups: (1) those which were nonresponsive to insulin, that is, the volume of distribution was unchanged by the injection of insulin; and (2) those sugars which were insulin responsive in that the volume of distribution was increased. In this latter group were placed d-galactose, l-arabinose and d-xylose. Levine called attention to the fact that the structure of these sugars with respect to carbons 1, 2, and 3 is similar and hence he concluded that the entrance of sugar into muscle "is governed by a transfer system which is specifically adapted with respect to chemical structure." Glucose itself cannot be used in Levine's eviscerated preparation because, unlike galactose, it is metabolized in the peripheral tissues. Therefore a constant blood level of glucose from which the volume of distribution

can be calculated is not established. However, Levine included glucose in the insulin-responsive group because the structure of its first 3 carbon groups is similar to that of the sugars experimentally shown to be insulin responsive.

Ross (*loc. cit.*) at the London Ophthalmological Institute approached the subject in a different way. Initially he was interested in studying the rate of penetration of a variety of chemicals from the blood stream into the aqueous humor through the ciliary body. He calculated his results in terms of a "permeability constant" and he compared this constant with the relative lipid solubility of the substance, that is, the ratio of its solubility in alcohol to its solubility in water. He found a striking correlation between these two variables. Those substances which had a high relative lipid solubility and therefore could be termed "lipophylic" had high permeability constants. Contrariwise, those that had a relatively low lipid solubility and therefore might be termed "lipophobic" had low permeability constants. From the striking correlation between these two variables in a large number of substances, Ross concluded that these relations were in accord with the concepts of cellular membrane structure as originally postulated by Overton. The cell membranes have lipid characteristics; accordingly, the greater the lipid solubility of a metabolite, the more readily does it enter the cell. Ross observed that among all the substances he studied glucose was an exception. It has a relatively low lipid solubility but a relatively high permeability constant. Some other factor must be involved in the ready penetration of glucose into the aqueous humor through the ciliary body and it was natural to suppose that insulin played some role here. Testing this hypothesis experimentally, Ross reported data which are illustrated in Figure 1. In the normal rabbit the permeability constant of glucose across the blood-aqueous barrier of the ciliary body was 200 in Ross's units. In the alloxanized preparation, characterized by high blood sugar

TRANSFER OF GLUCOSE ACROSS BLOOD-AQUEOUS BARRIER IN RABBIT EYE

(Ross, E. J., 1952)

	1000 k_{in}
Normal	199 ± 36
Alloxanized (Blood glucose 400-500 mg %)	102 ± 10
Decrease	97 ± 38
	t = 2.5

FIG. 1. Transfer of glucose across blood-aqueous barrier in rabbit eye. Data of Ross, 1952.

levels, the permeability constant was approximately 50% of that of the normal. Treatment of the alloxanized diabetic rabbit with insulin restored the permeability constant to normal values. On the basis of these findings Ross concluded that one function of insulin was to influence change in the permeability of the ciliary body to glucose.

Park (8, 9) and his coworkers were the first to obtain direct evidence that the transport of glucose across cell membranes was accelerated by insulin. They used the rat diaphragm, the heart, or the skeletal muscle *in vivo* and *in vitro* and by using isotopic glucose they were able to determine the intracellular free glucose, that is, glucose uncombined with phosphate as a hexose phosphate. Park et al. showed that in the presence of insulin, the concentration of free glucose, i.e., sugar uncombined with phosphate, within the tissue cells was higher than in the absence of insulin. From many experiments of this type, Park and his coworkers concluded: "that an action of insulin on glucose uptake is to accelerate a step concerned with the transport of glucose into the tissues. This step antecedes and is distinct from glucose phosphorylation by the hexokinase reaction."

This so-called transport hypothesis of the action of insulin with respect to glucose in skeletal and cardiac muscle has been amply supported by work of other authors. However, it cannot be generalized to apply to all other types of tissues, particularly the liver. In fact, as I shall point out subsequently, there is good evidence to indicate the contrary.

DEFECTS OF GLUCOSE METABOLISM IN THE DIABETIC LIVER

The defect of glucose metabolism in the diabetic liver is still subject to considerable divergences of opinion. However, in Figure 2 I present a summary of metabolic defects of glucose metabolism in the diabetic liver. Much of this evidence has been obtained by the study *in vitro* of liver slices from the diabetic rats or cats using isotopic glucose. In summary: The figure shows (1) there is a diminished uptake of glucose; (2) a diminished oxidation of glucose to CO_2; (3) a diminished conversion of glucose to glycogen, hence a diminished glycogen storage; (4) a depression of the ability of the liver to phosphorylate glucose; and (5) a markedly increased new formation of glucose, particularly from unknown precursors presumably protein. One can conclude from this evidence that a metabolic block in the early stages of metabolism of glucose exists in the liver of the diabetic animal. The exact nature of this metabolic block of glucose metabolism in the liver is not completely established. There is evidence that the permeability of liver cells to glucose is not influenced by insulin. Hence the metabolic block, unlike the case of the muscle, is not concerned with an inhibition of transport of glucose across the cell boundary. A considerable amount of work by Hastings' group (10) at Harvard is compatible with the hypothesis that the defect is concerned with the hexokinase reaction.

But there is also evidence to indicate that there is a second metabolic block in the diabetic liver causing decreased synthesis of fatty acids.

DEPARTURES FROM NORMAL OF THE GLUCOSE METABOLISM OF LIVER SLICES FROM ALLOXANIZED RATS

(COMBINED DATA FROM THE LITERATURE)

GLUCOSE UPTAKE	DECREASED
CONVERSION TO CO_2	DECREASED
GLYCOGEN FROM GLUCOSE	MARKEDLY DECREASED
GLUCOSE OUTPUT	MARKEDLY INCREASED
GLUCOSE FROM UNKNOWN SOURCES	MARKEDLY INCREASED

FIG. 2. Departures from normal of the glucose metabolism of liver slices from alloxanized rats. Combined data from the literature.

FATTY ACID METABOLISM IN THE DIABETIC LIVER

Our present knowledge of fatty acid synthesis or fatty acid breakdown is presented in a schematic way in Figure 3.

Higher fatty acids, for example, palmitic acid, a 16-carbon fatty acid, are broken down by successive beta oxidation. This process involves three steps: (1) activation of the fatty acid by condensation with coenzyme A, (2) oxidation at the beta carbon to form a beta-keto acid, and (3) a splitting off of the terminal two carbons to form acetyl-coenzyme A. The acid is now shorter by two carbons. A repetition of this process results in the step by step breakdown of the fatty acid to acetyl-CoA. In the liver, two fates of the acetyl-CoA are of immediate interest: (1) oxidation through the Krebs' cycle to carbon dioxide, or (2) a combination of two acetyl-CoA molecules to form a 4-carbon ketone which is not further metabolized in the liver.

The synthesis of higher fatty acids, e.g. palmitic acid, is indicated in the second half of the schema. There must be a precursor of acetyl-CoA. For example, glucose, lactate, pyruvate, fructose, or acetate. By a series of condensations and reductions acetyl-CoA molecules are built up step by step into longer

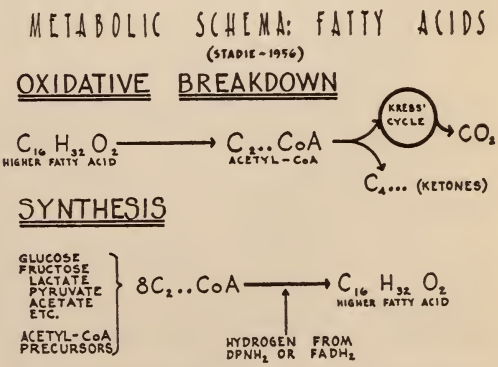

FIG. 3. Metabolic Schema: Fatty Acids. Data of Stadie, 1956.

and longer chains until the final product, palmitic acid, is synthesized. The H for reduction is furnished by reduced diphosphopyridine nucleotide, flavin adenine dinucleotide, or possible reduced triphosphopyridine nucleotide. But it is important to emphasize that the path of synthesis is not entirely the same as the path of oxidation. I shall return to this later.

In Figure 4 I show data taken chiefly from Chaikoff's (11) work. He equilibrated liver slices from diabetic rats with media containing various metabolites uniformly labeled with isotopic carbon. With glucose as the metabolite, no radioactivity is found in the CO_2, a result fully to be expected and indicating the presence of the first metabolic block at an early stage of glucose metabolism. In addition, there is no fatty acid synthesis from the glucose.

With isotopic fructose the production of CO_2 is the same as that observed in the normal rat. This means that the formation of acetyl-CoA from fructose is unimpaired in the diabetic. But there is no incorporation of this acetyl-CoA into higher fatty acids. The same findings are observed using isotopic acetate. Except in the case of glucose, these data clearly mean that we have all the conditions necessary for fatty acid synthesis, namely, acetyl-CoA formation and, since CO_2 is formed, reduced co-factors as sources of hydrogen for purposes of reduction. Nevertheless, higher fatty acids are not synthesized.

FATTY ACID METABOLISM OF SLICES OF LIVER FROM DIABETIC RATS

(DATA OF CHAIKOFF ET AL-1951)

ISOTOPIC NUTRILITIES	RECOVERED ISOTOPIC CARBON: AS CO_2	AS HIGHER FATTY ACIDS
GLUCOSE	O	O
FRUCTOSE	NORMAL	O
LACTATE	NORMAL	O
PYRUVATE	NORMAL	O
ACETATE	NORMAL	O

FIG. 4. Fatty acid metabolism of slices of liver from diabetic rats. Data of Chaikoff et al., 1951.

From the summation of this evidence, Chaikoff (12) concluded that: "A second biochemical block must therefore be postulated for the diabetic liver, and the observations with C^{14}-acetate indicate that it lies in the path of conversion of a '2-carbon-like' compound to fatty acids." This metabolic block, so clearly demonstrated in the liver slice of the alloxanized rat, may be eliminated in two ways: (1) by the prior dietary administration of fructose and (2) by the prior administration of insulin. But it is important to note that the results are not the same: Prior fructose feeding restores the ability of the liver slice to synthesize fatty acids from acetate, lactate and pyruvate but does not restore the loss of the ability of the liver slice to oxidize glucose or incorporate it into fatty acid. Insulin treatment, on the other hand, eliminates both metabolic blocks.

Consider these data in Figure 5 in relation to data obtained in studies on the metabolism of liver slices from depancreatized cats obtained in our laboratory and the laboratory of Gurin. Stadie, Zapp, and Lukens (13) studied the formation of ketone bodies by cat liver slices. Note the high rate of ketone formation (1200) in the case of the depancreatized cat as compared to normal (240). In the depancreatized-hypophysectomized (Houssay) cat ketone formation is reduced to practically zero. Compare the data with the rate of incorporation by liver slices of acetate into long chain fatty acid observed by Brady, Lukens, and Gurin (14). In the depancreatized cat this incorporation is es-

	ACETATE INCORPORATED BY CAT LIVER SLICES INTO LONG CHAIN FATTY ACIDS Brady, Lukens, and Gurin (1951)	KETONE FORMATION BY CAT LIVER SLICES Stadie, Zapp, and Lukens (1940)
	Mg / 100 mg Mean	Micromoles / Kg Cat Mean
Normal Cats	2 – 8	240
Depancreatized Cats	0 – 0.7	1200
Houssay Cats	5	85

FIG. 5. Fatty acid synthesis from acetate and ketone formation by liver slices from normal, depancreatized and Houssay cats. Data of Brady, Lukens and Gurin, 1951; and Stadie, Zapp and Lukens, 1940.

sentially zero but in the Houssay cat it is restored to normal (5). Both sets of data can only lead to one conclusion, namely, that the oxidative breakdown of higher fatty acids to acetyl-CoA from which the ketones are formed is unimpaired in the diabetic state; and second, that synthesis of fatty acids from acetyl-CoA is impaired. This must mean that in the diabetic the two pathways, namely, oxidative breakdown, and the synthesis of fatty acids must differ in some important detail.

Further experimental evidence that there are two pathways of fatty acid metabolism, one of which is impaired in the diabetic, is indicated by the data shown in Figure 6 from experiments by Shaw from Gurin's laboratory.

Shaw and Gurin (15) studied fatty acid synthesis by mitochondrial preparations made from liver of normal or diabetic rats. The system used consisted of four parts: (1) washed mitochondria either intact or lysed; (2) the supernatant from homogenized liver spun at high speed to remove all particulate matter; (3) certain co-factors such as magnesium, citrate, coenzyme 1 (indicated as DPN) and (4) a precursor of acetyl-CoA, namely, isotopic pyruvate. The figure shows that in the case of mitochondria from normal rat liver, fatty acid synthesis from the isotopic pyruvate occurs when normal liver supernatant is included in the system. But synthetic butyryl-CoA alone gives the same result. Synthesis of higher fatty acids from the pyruvate then occurred at a rate comparable to that observed with normal liver supernatant. With mitochondrial preparations made from diabetic rat liver, the addition of supernatant prepared from the diabetic liver resulted in no fatty acid synthesis from pyruvate. With normal liver supernatant added, fatty acid synthesis did occur. The same, however, was observed with butyryl-CoA alone. On the basis of these experiments, Shaw and Gurin concluded that: "butyryl-CoA appears to be able to replace the supernatant fraction of both the normal and diabetic water-soluble systems. It seems reasonable, therefore, to suggest that the diabetic liver is unable to convert pyruvate, acetate or acetyl-CoA to fatty acids, because it cannot convert acetyl-CoA to butyryl-CoA. This defect in the metabolism of the diabetic liver is presumably due to the inability of the soluble enzyme system to supply the co-factor or co-factors necessary for the reaction under discussion."

The scheme of fatty acid metabolism presented in Figure 7 is based upon the evidence that we have been discussing. Path I indicates the steps involved in oxidation. A higher fatty acid containing, let us say, 16 carbon atoms, is broken down by reactions involving successive condensation with coenzyme A and beta oxidation. A stepwise formation of acetyl-CoA occurs. In the liver the acetyl-CoA is either oxidized in the Krebs' cycle to CO_2 or by condensation of two molecules of acetyl-CoA produces a 4-carbon ketone body. As

FATTY ACID SYNTHESIS BY HEPATIC MITOCHONDRIA FROM NORMAL OR DIABETIC RATS

(DATA OF SHAW AND GURIN - 1956)

ADDED COFACTORS: Mg ; Citrate ; DPN
PRECURSOR OF ACETYL CoA: Isotopic Pyruvate

SOURCE OF MITOCHONDRIA	FURTHER ADDITIONS	FATTY ACID SYNTHESIS
NORMAL RAT LIVER	NORMAL LIVER SUPERNATANT	YES
	NONE	NO
	BUTYRYL-CoA	YES
DIABETIC RAT LIVER	NORMAL LIVER SUPERNATANT	YES
	DIABETIC LIVER SUPERNATANT	NO
	BUTYRYL-CoA	YES

FIG. 6. Fatty acid synthesis by hepatic mitochondria from normal or diabetic rats. Data of Shaw and Gurin, 1956. Added cofactors: Mg; citrate; DPN. Precursor of acetyl CoA: Isotopic pyruvate.

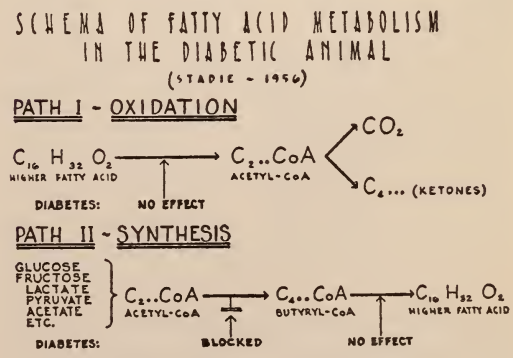

FIG. 7. Schema of fatty acid metabolism in the diabetic animal. Data of Stadie, 1956.

we have seen from our data with the diabetic cat, the production of ketone bodies proceeds at a very rapid rate and therefore the enzyme systems and the necessary co-factors for this pathway are unimpaired by the insulin lack in the diabetic animal.

Pathway II shows the synthesis of higher fatty acids from acetyl-CoA precursors such as glucose, fructose, lactate, pyruvate, acetate, etc. As we have seen from the data of Chaikoff, acetyl-CoA formation (except from glucose) is unimpaired in diabetic liver slices. But the ability of acetyl-CoA to engage in the successive reactions of condensation and reduction with the final production of higher fatty acids is impaired. The work of Shaw and Gurin makes it reasonable to assume that the jump from acetyl-CoA to butyryl-CoA is a possible diabetic defect which is the cause of failure of fatty acid synthesis. Recently, Langdon (16) has also published data from which he concluded that the pathways of oxidation and synthesis of fatty acids are different. One step in the oxidation required oxidized flavin adenine nucleotide (FAD) as a co-factor; but the reversal of this step in synthesis required not reduced flavin adenine nucleotide ($FADH_2$) but reduced triphosphopyridine nucleotide ($TPNH_2$) as the co-factor. The analogous reactions as the chain lengths of the fatty acid CoA derivatives increase are also dependent upon $TPNH_2$. $TPNH_2$ formation is dependent upon adequate carbohydrate metabolism. Thus the relation between diminished glucose oxidation in the diabetic and failure of fatty acid synthesis is suggested.

Returning for a moment to Figure 5, the evidence here indicates strongly that the system which functions to bridge this gap between acetyl-CoA and butyryl-CoA is impaired in the diabetic state because of the inhibitory action of pituitary factors which become manifest owing to the lack of insulin. In the hypophysectomized-depancreatized animal, the incorporation of acetate into higher fatty acids is restored to the normal state. In other words, in the Houssay cat the removal of the pituitary factor has restored the ability of the diabetic liver slice essentially to its full synthesizing capacity with respect to fatty acids. Note further that in the Houssay preparation ketone formation falls to zero indicating that the normal balance between synthesis and oxidation of fatty acid has been restored and homeostasis of fat metabolism of the liver has been re-established. It is a possible conclusion then to state that the enzyme system bridging the gap from C_2 to C_4 in fatty acid synthesis must be under balanced control of both insulin and pituitary factors. Whether these effects are entirely dependent upon a restoration of carbohydrate metabolism in the liver, as the experiments of Langdon suggest, remain undetermined.

PHOSPHATE METABOLISM IN THE DIABETIC ANIMAL

It is now well established that the oxidation of certain metabolites by the Krebs' cycle brings about the incorporation of inorganic phosphate into energy-rich types of organic combination, for example, adenosine triphosphate. The reactions involved in the formation of these energy-rich phosphate compounds are collectively grouped under the term "oxidative phosphorylation." The compounds formed become sources of chemical energy for a wide variety of metabolic activities. Much evidence in the literature makes it reasonable to assume that a deficient formation of these energy-rich phosphate bonds may play a role in the metabolic defects of the diabetic animal.

It is fairly well established that oxidative phosphorylation occurs exclusively in the mitochondria. Is this activity of the hepatic mitochondria impaired in the diabetic animal? Vester (17) in our laboratory studied the possible existence of this defect in the diabetic animal by measurements of oxidative phosphorylation in isolated mitochondria prepared from the livers of depancreatized cats. The mitochondria were prepared by the customary method of differential centrifugation of liver homogenates. They were

equilibrated aerobically in suitable media containing pyruvate as a source of energy and a glucose-hexokinase system to bind the ATP as soon as it is formed.

I show a summation of his data in two figures. Figure 8 compares: (1) oxidative phosphorylation as measured by the rate of formation of adenosine triphosphate, and (2) the phosphorus to oxygen ratio of mitochondria isolated from the livers of a series of normal and depancreatized cats. The rate of formation of ATP by the mitochondria from the livers of the diabetic cats (as shown in the left hand column) is significantly diminished compared to that observed in the normal animal. The values are 77 and 19 respectively. In the right hand column are shown the so-called P:O ratios in both instances. The P:O ratio is the ratio between the amount of ATP formed by the mitochondria and oxygen uptake. This ratio measures the efficacy of oxidative phosphorylation by the mitochondria. When the P:O ratio is zero, for example, the oxidative processes occurring in the mitochondria have not been coupled to reactions converting the low energy adenosine diphosphate and inorganic phosphate to the higher energy compound, adenosine triphosphate. In other words, the energy of oxidation of the metabolite in the mitochondria has been wasted as heat instead of being stored as adenosine triphosphate for future use. The maximum value P:O expected in the normal animal is of the order of 3.0. In Vester's experiments, the normal mitochondria yielded a mean value of about 2.4 whereas the mitochondria from the diabetic cats gave a significantly lower mean value in 6 animals of 1.1. Both the low ATP values and the low P:O ratios indicate that the ability of the mitochondria to generate high energy phosphate bonds in the form of adenosine triphosphate is diminished in the diabetic.

Vester also showed that these manifestations of impairment of oxidative phosphorylation in the diabetic cat can be reversed by prior treatment of the diabetic cat with insulin. His experiments were done in the following way. Two or three days after pancreatectomy a liver biopsy was done. Mitochondria were prepared and tested for phosphorylative capacity. Then the cat was vigorously treated with insulin for a period of two or three days and restored essentially to normal and a second specimen of liver obtained. As before, mitochondria were prepared and assayed for oxidative phosphorylation. Figure 9 shows the data obtained in a series of 8 depancreatized cats. In the left hand column, the solid column indicates the total oxidative phosphorylation as measured by ATP formation

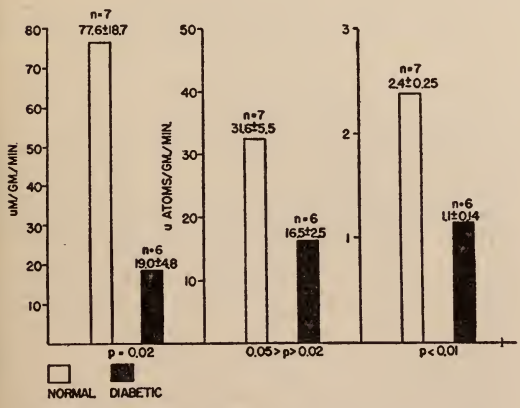

FIG. 8. Oxidative phosphorylation by hepatic mitochondria from normal and diabetic cats. Data of Vester and Stadie, 1957.

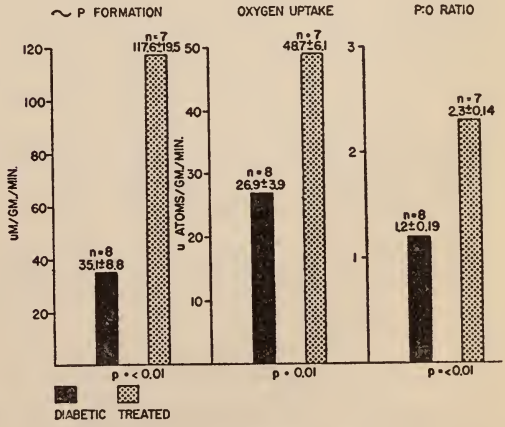

FIG. 9. Restoration to normal of the oxidative phosphorylation by mitochondria prepared from livers of insulin treated depancreatized cats. Data of Vester and Stadie, 1956.

in the diabetic state; the hatched column in the restored state. It is clear that the insulin treatment has restored oxidative phosphorylation in the isolated mitochondria essentially to normal. The P:O ratio which is shown on the right of the slide is also restored to normal.

The summation of Vester's evidence which I have cited here, together with that in the literature, indicates that oxidative phosphorylation is impaired in the diabetic status and this impairment cannot be ignored as a possible factor for departures of both fat and carbohydrate metabolism from normal.

METABOLIC ADAPTATION BY INSULIN

Recently attention has been focused upon a phenomenon which might be called metabolic adaptation brought about by insulin. By adaptation I mean that in the presence of insulin a change in the function of enzymatic systems of tissues occurs which requires considerable time for full development. This phenomenon has been well summarized by Hastings (18) and his coworkers who studied it at considerable length. Their results in the case of the diabetic rat are shown in Figure 10. Using the diaphragm as an example of muscle, they showed that the response of injected insulin was immediate. A minute or less after the injection into the intact rat the animal was sacrificed and the diaphragm rapidly removed. In this brief time, the diaphragm had responded to the insulin as shown by the fact that when it was equilibrated *in vitro* in a medium containing glucose, it showed a significant increase of glucose uptake and glycogen synthesis compared to control series of diaphragms obtained from rats without prior insulin injection. Liver slices, obtained from the same rats, responded to the injected insulin so slowly that treatment periods of 6–24 hours were required for full restoration to the normal from the diabetic status. As measures of response to insulin Hastings quoted among other effects the total phosphorylation of glucose, the incorporation of fructose, pyruvate, or acetate into higher fatty acids. The responses in the case of the liver are strikingly different from those of the muscle. Insulin reaction in the diaphragm is essentially instantaneous and appears to be concerned with the transport of glucose. In contrast, insulin action in the liver is slow and in the diabetic can only be demonstrated by injection into the intact animal. A reasonable hypothesis would be to assume that by some mechanism which at present is not known, insulin permits the liver slowly to complete an enzyme system which in the absence of insulin has lost its function in whole or in part. The adaptation requires perhaps synthesis of new proteins or the formation of co-factors. These reactions take time and further suggest the possibility of diverse types of insulin action in the liver affecting glucose or fatty acid metabolism.

On the basis of these considerations, it is

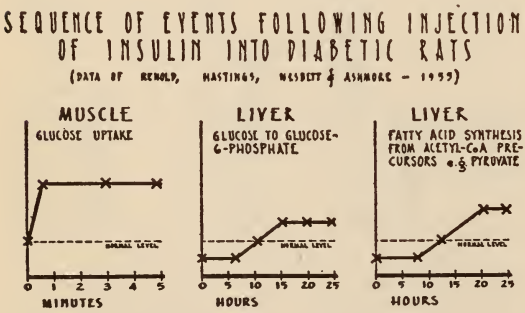

FIG. 10. Sequence of events following injection of insulin into diabetic rats. Data of Renold, Hastings, Nesbett, and Ashmore, 1955.

UNIFIED CONCEPT OF INSULIN ACTION
(STADIE - 1956)

TISSUE	MECHANISM OF ACTION	SITE OF ACTION	CHIEF METABOLIC EFFECTS
MUSCLE	COMBINATION	CELL SURFACES	GLUCOSE TRANSPORT et seq.
LIVER	ADAPTATION	ENZYME SYSTEMS: CONTRA PITUITARY	GLUCOSE OXIDATION, etc; FATTY ACID SYNTHESIS; OXIDATIVE PHOSPHORYLATION (?)
ADIPOSE	ADAPTATION	ENZYME SYSTEMS	GLUCOSE OXIDATION, etc; FATTY ACID SYNTHESIS
BRAIN	NO DEMONSTRATABLE ACTION		
OTHER	INSUFFICIENT DATA		

FIG. 11. Unified concept of insulin action. Data of Stadie, 1956.

possible to formulate, as a working hypothesis what might be called a unified concept of insulin action. I show this in Figure 11. Four columns are considered: (1) tissue; (2) mechanism of action; (3) site of action; and (4) chief metabolic effects. In muscle, the mechanism of action may be considered to be a combination of insulin with the muscle and the site of the action perhaps upon cell surfaces. The main metabolic effects would be an increase of glucose transport which of course would accelerate phosphorylation and therefore further reactions. In the liver adaptation is necessary, time is required, the enzyme systems are under the contra control of pituitary factors, and the chief metabolic reactions involved are glucose oxidation, fatty acid synthesis, oxidative phosphorylation and perhaps others. In adipose tissue, the situation is about the same as that outlined for the liver. In the brain, as many experimenters have found, there is no demonstrable action of insulin. In other tissues the data available is insufficient to make discussion profitable. This unified concept of insulin action need not be complete nor even free of errors so long as it has some meaning to the experimenter and is provocative of further experimentation.

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Observations on Antibiotic Resistance of Certain Pathogenic Bacteria[1]

By MAXWELL FINLAND, M.D.[2]

I CAN assure you that I consider it a great pleasure and honor to have been chosen to present this 75th Mary Scott Newbold Lecture. It made me feel humble indeed to see the roster of eminent physicians who have preceded me in this Lectureship. However, in this city, which is so well known for its pride in its traditions and in its famous families and institutions, I may perhaps be pardoned if I mention that I took particular notice of the fact that this is the eighth of these lectures by a member of the faculty of the Harvard Medical School, and that both the present director of the Thorndike Memorial Laboratory and his predecessor are among those whom you have previously honored in this manner.

During the past few years, as new and useful antibiotics became available, my associates and I took the opportunity to test those agents for their activity against some of the common varieties of pathogenic bacteria encountered in the hospital. From time to time we also collected additional groups of strains of selected species of pathogenic bacteria from current cases and tested them for their susceptibility not only to the newly introduced antibiotics but, also with antibiotics that had already been in wide use. This was done in order to learn whether there had been any changes in the susceptibility of such organisms to these widely used agents. This paper will deal primarily with the results of these studies and their implications. No attempt will be made to review the vast literature on resistance or to discuss all the possible mechanisms involved.

Recovery from infections may involve many humoral or cellular factors within the host, but the beneficial action of antibiotics in this recovery, according to our present understanding, depends primarily if not entirely on their action in inhibiting the growth and multiplication of the microbial pathogens or in actually killing them. The clinical significance of the data to be presented is based on the premise that changes in the susceptibility of microorganisms to the antibiotics *in vitro* will necessarily be reflected in corresponding alterations in the effectiveness of these antibiotics in the treatment of the infections which they produce.

The comparisons to be presented have some added validity in that the tests were carried out, by the same method throughout. This method employs a series of plates of suitable nutrient agar into which 2-fold dilutions of antibiotics are incorporated. A loopful of each of several freshly grown cultures are streaked onto segments of the surface of these plates, which are then incubated and observed for growth. The minimum concentration of antibiotic in the plate on which there is complete inhibition of visible growth is taken to represent the sensitivity of that strain. For each species, the per cent of the strains inhibited by the various concentrations of each antibiotic is charted on a cumulative distribution curve. The curves for all of the antibiotics when charted together constitute what may be called the "antibiotic spectrum" of that species. This is essentially the reverse

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of the usual antimicrobial spectrum of any given antibiotic, which represents the relative susceptibility of different microorganisms to that antibiotic.

As one simple illustration of the method and results, we accumulated a series of capsulated, type-specific pneumococci that were isolated prior to 1949 and tested them with 7 antibiotics that were available at that time (1) which included 2 forms of polymyxin, one of which (polymyxin D) is no longer available. All of the strains exhibited an essentially uniform susceptibility to each antibiotic, within the limits of error of the test. There were no variations in susceptibility among the different specific types. However, the susceptibility of all strains to the different antibiotics varied widely as could be seen from the arrangement of the curves representing those antibiotics. Penicillin was far more active, on a weight basis, than all of the others, chlortetracycline (Aureomycin) ranked second, followed by chloramphenicol (Chloromycetin), bacitracin and streptomycin; the polymyxins were essentially inactive.

In 1954 and 1955 another series of type specific pneumococci were collected from similar cases in the same hospital and tested with 11 antibiotics, including all those previously used, except polymyxin D (2). The shape and position of the 6 curves representing the antibiotics previously used were identical with those observed in 1949, indicating that there had been no change in the susceptibility of freshly isolated pneumococci to the antibiotics that had been in use during the intervening period.

In the first of these studies (1) it was shown that strains isolated after January 1948 were just as sensitive to penicillin G as those isolated and tested before 1945. The second study also indicated that erythromycin was nearly as active as penicillin against the pneumococci, that the 3 tetracycline analogues were equally active and were still much more active than chloramphenicol in spite of the fact that the latter had been used only to a very limited extent, whereas the tetracyclines had been used very extensively in our hospital up to that time.

We have now had the opportunity to study strains of a number of different species in this manner, but only the more interesting results obtained with a few of them will be considered. Among them the pathogenic staphylococci were studied most intensively and revealed the most marked changes.

Staphylococci isolated and tested before July 1949 with the 7 antibiotics then available yielded a different type of spectrum when compared with that of the pneumococcus (3). The strains varied markedly in their susceptibility to penicillin; a large proportion were highly sensitive, but many were highly resistant. Therewas also moderate variation in the susceptibility of the strains to streptomycin and a small proportion of them were also significantly less sensitive than the rest to chlortetracycline. All were uniformly sensitive to chloramphenicol and bacitracin and uniformly resistant to the polymyxins.

A breakdown of the strains into those isolated before and after 1946 revealed that prior to that year more than 80 per cent of the strains were inhibited by 0.04 microgm. per ml. or less and only a rare strain required more than 5 microgm. per ml. By contrast, less than 40 per cent of strains isolated after 1946 were inhibited by 0.1 microgm. per ml. and more than 30 per cent required 25 microgm. or more per ml. The year 1946 will be recalled as the time when penicillin became commercially available and its intensive use became widespread.

At this time there was also evidence strongly suggesting that originally susceptible staphylococci may become resistant to penicillin in the patient during treatment with that antibiotic. This was difficult to demonstrate decisively, but in 4 patients with bacterial endocarditis studied before 1949 and in whom introduction of new strains from outside could be virtually excluded successive isolations from blood cultures or at autopsy yielded staphylococci of progressively increasing resistance.

Comparisons with other groups of staphy-

lococcal strains isolated at the same hospital through 1953 (4) showed a progressive decrease in the proportion of highly sensitive strains and a corresponding increase not only in proportion of resistant strains but in their degree of resistance to penicillin. Most of the change took place before 1953; a group of strains isolated at the end of that year did not differ materially from those isolated in 1951 and 1952.

Most of the groups of strains studied were randomly collected from patients with infected lesions, but 2 selected series of strains collected in our laboratory by Dr. George Gee Jackson illustrated the further effects of hospitalization and antibiotic therapy. One was a group of staphylococci isolated as the only or predominant organisms in cultures from 50 of 166 consecutive autopsies performed at the Boston City Hospital in the spring of 1950. Only 6 of these 50 strains were from patients who had not received antibiotics during their last illness and these were the only ones that were sensitive to penicillin; the entire group of strains was generally more resistant than the other unselected groups studied.

A further series of 44 strains were isolated in 1951 from feces of patients with gastroenteritis; only 5 of these patients had received no antibiotics and the rest had been under treatment with oxytetracycline or chlortetracycline. This was the most resistant group of strains studied, the only penicillin sensitive ones among them being those obtained from the patients who had not been exposed to antibiotics.

Changes in susceptibility to chlortetracycline and especially to oxytetracycline were very similar, although the proportion of strains resistant to these antibiotics was much less than to penicillin. Oxytetracycline had only become available late in 1950 but staphylococcal strains resistant to chlortetracycline already exhibited similar or even greater resistance to oxytetracycline. By 1952, about 30 per cent of the staphylococcal strains isolated from all infected sources were highly resistant to chlortetracycline and a slightly higher proportion was resistant to oxytetracycline. A much greater proportion of the autopsy strains were resistant to these agents, especially to oxytetracycline and nearly all of the fecal strains studied in 1951 were highly resistant to that agent.

With chloramphenicol which had been used only sparingly and selectively during all this time, no such changes in resistance of staphylococci were evident and the same was true of bacitracin. Also there had been only a minor change in the susceptibility of staphylococci to streptomycin, which had also been used rather selectively, and usually only in combination with other antimicrobial agents, particularly penicillin.

These findings are clearly illustrated in the antibiotic spectrum of a series of 500 consecutive strains of pathogenic staphylococci isolated at the Boston City Hospital during 1951–1952, just prior to the introduction of erythromycin (5). At this time there was shown to be a fairly sharp cleavage between strains that were highly sensitive to penicillin—less than 25 per cent of the total—and nearly all the rest which were highly resistant, with only a few exhibiting intermediate susceptibility. The same was true for chlortetracycline and oxytetracycline, except that the proportions of strains sensitive to these antibiotics were about 70 and 60 per cent, respectively. The strains were nearly uniform in their susceptibility to each of 6 other antibiotics, none of which had been used as widely or as intensively. In particular, nearly all of the strains were inhibited by 0.4 microgm. per ml. of erythromycin and none required more than 1.6 microgm. per ml. of that antibiotic to produce complete inhibition.

A study of the ability of these 500 strains to produce the penicillin destroying enzyme penicillinase was made by a simple method (6); this involved streaking the cultures of staphylococci on the surface of agar which had been inoculated with a highly sensitive strain of *Sarcina lutea* and also contained a

completely inhibiting concentration of penicillin for that strain. Penicillinase production is clearly evident by the halo of colonies of Sarcina growing in the agar under and around the heavy surface growth of the staphylococcus. By this method all of the penicillin-sensitive staphylococci,—those that were inhibited by 1.6 microgm. per ml. or less, failed to produce penicillinase, and the more resistant ones, which required 12.5 microgm. per ml. or more, all produced the penicillin-inactivating enzyme. There were only a few irregular results in the intermediate range of concentrations.

These results suggested that there are essentially 2 varieties of staphylococci distinguishable by their ability to produce penicillinase. *In vitro*, although it is possible to produce highly resistant staphylococci following repeated exposures of sensitive, non-penicillinase producing staphylococci to penicillin, such resistant strains do not produce penicillinase. On the other hand all resistant strains isolated from infected sources are penicillinase producers. It may, therefore, be concluded that the increased occurrence of penicillin-resistant strains may be the result of the elimination of the sensitive, non-penicillinase producers by the widespread use of penicillin with their consequent replacement by resistant penicillinase-producing strains.

Recently, Geronimus and Cohen (7) have demonstrated that a relatively sensitive strain that produces only a small amount of penicillinase can, by exposure to subinhibitory concentrations of penicillin *in vitro* or *in vivo*, be induced to increase its resistance to penicillin and concomitantly to increase its penicillinase production. Such a mechanism may account for the large proportion of strains in the intermediate range of resistance as observed between 1946 and 1949 and for the rare occurrence of such strains in this hospital since then, after the long period of intensive exposure of the hospital population, and even of the general public to penicillin. Although enzymes that inactivate the tetracyclines have not been clearly demonstrated, some similarly selective mechanism appears to have been operative among staphylococci with respect to the appearance and persistence of strains of staphylococci resistant to these agents following their widespread use.

The significance of these findings in therapy may be illustrated from clinical experience. In a patient observed in 1952 (Case 9, ref. 6), a blood culture obtained before any antibiotics were given yielded a staphylococcus that was highly sensitive to both penicillin and oxytetracycline. After 4 days of treatment with penicillin, a second blood culture also yielded a staphylococcus, which was equally sensitive to oxytetracycline but this one was highly resistant to penicillin. After another 4 days during which both antibiotics were administered staphylococci grown from the blood and from an abscess were highly resistant to both antibiotics. The abscess was in a wound at the site of a repair of an arteriovenous fistula and there presumably were reinfections or mixed infections with various staphylococcal strains, the resistant ones being selected out and persisting as the sensitive ones were eliminated by the therapy.

In patients with pneumococcal pneumonia observed in 1951, treatment with oxytetracycline (8) resulted in the rapid elimination of the pneumococci, but the prevalent hospital strains of antibiotic resistant staphylococci often replaced the pneumococci of the sputum and multiplied freely, giving rise to suppurative staphylococcal complications, occasionally with bacteremia; this was often accompanied by severe acute staphylococcal enterocolitis that was sometimes fatal. In the latter cases, the nearly complete elimination of the basic flora of the bowel resulted in rapid multiplication of the resistant staphylococci which could then be seen and cultivated from the feces essentially in pure culture. Fortunately this severe type of staphylococcal enterocolitis has been quite infrequent since 1953 when the use of tetracycline largely replaced that of its earlier congeners at this hospital.

Our early studies with erythromycin indi-

cated that staphylococci acquire resistance to this antibiotic very rapidly during exposure to it both *in vitro* and *in vivo* (9). Studies by Lepper *et al.* (10) in Chicago, indicated clearly that the intensive use of erythromycin in hospital wards resulted in a rapid increase in the per cent of erythromycin-resistant staphylococci and in the degree of resistance of such strains cultured from patients and hospital personnel and a loss of effectiveness of this agent in treatment of infections. Concurrently there was some decrease in the per cent of staphylococcal strains resistant to penicillin which the erythromycin had replaced, and an increase in the proportion that were resistant to chlortetracycline, which was used more frequently as erythromycin lost its effectiveness. After the use of erythromycin was discontinued, the proportion of erythromycin-resistant strains dropped precipitously and there was again an upswing in the incidence of penicillin-resistant strains with the resumption of the use of that antibiotic.

There is marked and essentially complete cross-resistance among the erythromycin-like antibiotics, which include carbomycin, oleandomycin and spiramycin, following repeated exposures of staphylococci to any one of these agents *in vitro* (11); however, among strains isolated from patients such cross-resistance is demonstrable less regularly and is less complete (12). On the other hand, the intensive clinical use of spiramycin in a study by Lepper *et al.* (13) was accompanied by a significant increase in the proportion of strains of staphylococci that were resistant to both spiramycin and erythromycin. This was later observed to occur in the same clinic even when spiramycin was given only in combination with novobiocin, an antibiotic that had not previously been used in those wards (14).

Strains of staphylococci resistant to chloramphenicol may also increase in incidence during intensive use of that agent. This was illustrated in the experience of Gibson and Thompson (15) in Richmond, when they discontinued the use of chlortetracycline in the management of their burn wounds and used only chloramphenicol for a period of 6 months. During this time, the proportion of chloramphenicol-resistant staphylococci increased from about 15 to over 50 per cent and then fell again with equal rapidity when treatment with chloramphenicol was stopped and the use of chlortetracycline was reintroduced. This, however, resulted in another sharp increase in the proportion of strains resistant to chlortetracycline.

Resistance of staphylococci to novobiocin increases very rapidly during exposures to it *in vitro* (16) and experiences with its clinical use has indicated that such resistance may also develop fairly rapidly during treatment (17, 18).

Among the attempts to prevent or decrease the development of antibiotic resistance of staphylococci, the most successful has been the use of combinations of antibiotics, to each of which the organism is originally sensitive. Numerous combinations of the antibiotics in common use may serve to delay the development of resistant staphylococci and depress the degree of resistance that develops. One of the effective antibiotics for this purpose, among those in wide use, is chloramphenicol; although most strains of staphylococci are only slightly or moderately sensitive to this agent, they develop resistance to it quite slowly *in vitro* (19). This, plus the fact that they had been used sparingly in our hospital, has led to the choice of chloramphenicol plus erythromycin for the treatment of infections due to staphylococci that are resistant to both penicillin and the tetracyclines, and this still appears to be a useful combination.

Recently, however, we found that the *in vivo* activity resulting from the oral use of this combination is less than that obtained with oral erythromycin alone, at least as judged from the inhibiting activity of the plasma (20). This decreased activity is nevertheless acceptable in order to prolong the effectiveness of erythromycin. Other studies suggest that bacitracin or neomycin, which are more bactericidal in their action may be more effective agents to

use in combination with erythromycin or novobiocin, both to enhance activity and to delay the emergence of resistance.

In all such uses of antibiotic combinations, it must be emphasized that each of the antibiotics must itself be active against the infecting strain at the start in order to exert any favorable effect either on activity or on resistance. For example, as much as 200 microgm. per ml. of penicillin constantly present in a culture medium failed to prevent the rapid development of resistance to erythromycin and streptomycin during exposure to these agents of staphylococci that were originally highly resistant to penicillin (21).

Strains of the 3 major varieties of streptococci isolated in 1949 were tested for their susceptibility to each of the 7 antibiotics available at that time (22). The hemolytic streptococci, of which only those of group A were studied at that time, yielded an antibiotic spectrum similar to that of the pneumococci, except for the greater activity of bacitracin against the streptococci. There was a striking uniformity in the susceptibility of the different strains of these group A hemolytic streptococci to each of the antibiotics. Streptococci of the viridans behaved in nearly the same manner but were slightly less susceptible to penicillin and less uniformly so, and this was even more true of the enterococci which also varied somewhat in their susceptibility to some of the other antibiotics.

When strains of hemolytic streptococci of groups other than D were collected in 1954–1955 and tested with the same 6 antibiotics the results were essentially identical except with bacitracin; to this antibiotic the strains showed considerable variation in susceptibility. However, the recent series included many strains of groups other than A. When the strains of the different serologic groups were charted separately, it was observed that those of group A were just as susceptible as in the earlier study but strains of the other groups were appreciably less sensitive and showed greater variations in their susceptibility (23).

A similar study with enterococci collected during 1954–1955 (24) showed a somewhat wider variation in the susceptibility of the strains to penicillin, but the most striking difference as compared with the earlier study was in the susceptibility to the tetracyclines and to streptomycin. Whereas the earlier study showed only minor variations in susceptibility of the different strains to chlortetracycline and streptomycin, there now was a sharp break in the curves representing these antibiotics with only about 40 per cent of strains being sensitive and the rest highly resistant to chlortetracycline and about one-half of the strains being slightly sensitive to streptomycin and the rest highly resistant to that agent. The findings with oxytetracycline and tetracycline were similar to those with chlortetracycline. When the data for the recent strains were broken down according to the different species of enterococci, it was seen that those of *Str. liquefaciens* were predominantly sensitive, those of *Str. zymogenes* were mostly resistant whereas the strains of *Str. fecalis* were equally divided; this relationship held for each of the 3 tetracyclines and streptomycin. The overall changes in sensitivity of the enterococci may, therefore, be related, in part at least, to a change in the frequency with which the various species are being encountered rather than an increase in the resistance of originally sensitive strains. This, however, has not been firmly established.

We have not as yet adequately restudied the viridans group of streptococci, but data from the New York Hospital indicate that there had been no significant change in the average range of sensitivity to penicillin of strains isolated from cases of subacute bacterial endocarditis over the 10-year period from 1944 through 1953 (25). Likewise, the daily use of a penicillin dentifrice over periods of 1 or 2 years has not resulted in the appearance of penicillin-resistant strains of the usual species of viridans streptococci cultured from the mouth (26). However, after the use of penicillin a greater proportion of the strains were slightly less

sensitive than before but all were still inhibited by the same range of concentrations.

Two studies were carried out with freshly isolated gonococci, one on strains isolated in 1949 or earlier (27) and the other on strains obtained in 1953–1954 (28). The same 8 antibiotics and sulfadiazine were used in both studies and 3 additional antibiotics that had become avilable in the interim were used in the later one. These studies revealed no significant changes in the susceptibility of the strains to penicillin or to any of the other popular antibiotics and all strains were quite uniform in their susceptibility to each antibiotic. In the second series, however, a much smaller proportion of the strains were sulfadiazine-resistant and more of them were sensitive to the sulfonamide as compared with the strains studied in 1949. This may have been the result of the marked decrease in the use of sulfonamides and the more general use of antibiotics, particularly penicillin, in the treatment and prevention of gonococcal and other infections. It is also of interest that strains of gonococci isolated during penicillin treatment from apparent failures, or during relapses, or from patients who were slow to respond to treatment, were just as sensitive as strains obtained before treatment from patients in whom the disease was rapidly cured.

A study of strains of meningococci collected in 1953–1954 showed all of them also to be highly sensitive to penicillin and there was no change in susceptibility to this antibiotic when compared with strains tested in 1945 (29). The recent strains were quite uniformly susceptible to all other antibiotics but were moderately resistant to polymyxin, and even more so to bacitracin. In the *in vitro* test employed they were also sensitive to sulfadiazine; a few that appeared to be less sensitive by this test proved to be just as susceptible as the others in a mouse protection test carried out by Dr. Sara Branham at the National Institute of Health (30).

Strains of *Hemophilus influenzae* were studied first in 1949 (31) and again in 1954 (32). On each occasion all strains were susceptible to a narrow range of concentrations (6.3 microgm. per ml. or less) of all of the antibiotics with which they were tested, except for bacitracin, to which all strains of both series were resistant. Also in the second series all of the strains required 25 to 50 microgm. of carbomycin to produce complete inhibition of growth.

A few observations on antibiotic resistance among the Enterobacteriaceae may be of interest in view of the importance of these organisms in urinary tract infections and the increasing difficulties in controlling such infections. It was early noted that susceptible gram-negative bacilli readily acquire resistance to streptomycin during repeated subcultures in the presence of this antibiotic either in broth or on agar. On the solid medium, occasional colonies of completely resistant organisms appear during early subcultures (33).

In the treatment of pyelonephritis with streptomycin, strains of high resistance often emerge within the first 2 or 3 days of treatment, even when large doses are used, and these organisms persist (34). In such cases the urine is generally very acid. Streptomycin, however, was shown to be much more active in an alkaline than in an acid medium, its activity being increased some 40 to 80-fold over a range of pH that is attainable in the urine (35). Alkalinization of the urine before and throughout treatment with streptomycin resulted more frequently in rapid clearing of the bacteria, and even when there was a delayed bacteriologic relapse, the organisms that reappeared were as sensitive to streptomycin as the pretreatment ones. The overall results of streptomycin treatment of urinary tract infections were markedly improved with this method (36).

Some observations made on strains of Proteus and Pseudomonas (37–39) are also of interest. The strains of Proteus collected and studied in 1949 and earlier were not classified as to species (37). The majority of them were susceptible to chloramphenicol, streptomycin and chlortetracycline, in that order. However, a significant proportion of them were highly

resistant to penicillin and streptomycin, and rather high concentrations of chlortetracycline were required to inhibit most of them. Bacitracin was totally ineffective and the polymyxins were essentially inactive. Proteus was the only one among the pathogenic gram-negative bacilli studied that was resistant to polymyxin (37).

Against the strains of *Pseudomonas aeruginosa* collected and studied in 1949 and earlier (37), the polymyxins were the most active. Streptomycin was active in moderately high concentrations against most of these strains but a significant proportion was resistant to this agent. Chlortetracycline and chloramphenicol were inhibitory only in high concentrations that could not be attained by systemic treatment. All of these strains were resistant to penicillin and bactitracin.

When strains of Proteus were collected and tested in 1953–1954 (38), the antibiotic spectrum had apparently changed to an appreciable extent. There appeared to be a decrease in the proportion of strains sensitive to penicillin and chlortetracycline and some increase in resistance to chloramphenicol. However, a breakdown of the strains according to species revealed more striking differences. Strains of *P. mirabilis*, the only ones which do not produce indole, were moderately or highly resistant to chlortetracycline and to oxytetracycline but appreciably more susceptible to tetracycline. Strains of *P. vulgaris* were susceptible, and equally so, to all 3 tetracycline analogues and those of *P. vulgaris* and *P. rettgeri* varied, some being sensitive and others resistant to all 3 analogues. Susceptibility to penicillin was also related to species; strains of *P. mirabilis* varied from moderately sensitive to highly resistant, while those of the other 3 species were all resistant. Strains of *P. mirabilis* were somewhat more susceptible to streptomycin and chloramphenicol than were those of the other species, of which a greater proportion were resistant to these 2 antibiotics. Strains obtained from patients after treatment with tetracycline drugs were usually resistant to those agents. It also appeared likely that most of the other differences observed in the 2 series represented selections of resistant species rather than a true increase in resistance of originally susceptible strains.

Strains of *Ps. aeruginosa* were also studied in 1954 (39). Again, polymyxin was the most active agent, and no strains of increased resistance were encountered. Against the strains of this species, oxytetracycline was appreciably more active than tetracycline or chlortetracycline and there appears to have been an increase in the proportions of strains resistant to the latter and to streptomycin as compared with those observed in the earlier series. Almost all of the strains in both series were resistant to chloramphenicol. However, there did not appear to be any clear correlation between resistance of the strains and prior treatment of the patients from whom they were obtained.

A comparison of the susceptibility of strains of the same species isolated before and after antibiotic treatment of urinary tract infections was presented recently by Garrod and his coworkers (40). Nearly all were equally sensitive and only about 7 per cent of the strains they isolated after treatment were significantly more resistant than the corresponding strains isolated before treatment. Their findings, as well as most of our own and those from many other clinics suggest that the major result of antibiotic therapy is the selection of species and variants of increased resistance which are permitted to survive and multiply rather than to cause a true increase in resistance of originally susceptible strains.

It can be concluded from these and other studies that the major result of the widespread use of antibiotics is the elimination of the more sensitive bacterial flora and its replacement by one that is resistant to the antibiotics that are intensively used. This is particularly true with respect to staphylococci and is most important in hospital populations; it is also important with regard to the coliform and other organisms encountered in urinary tract infections. Fortunately many important and highly sensitive species of pathogenic bacteria show little if any variation in their susceptibility to the

useful antibiotics and have exhibited no recognizable change in their susceptibility to these agents during the last few years.

Changes in resistance of originally susceptible organisms during treatment is probably of minor significance in the overall picture, but it may be of the greatest importance to the individual patient. Such changes are important primarily with respect to certain antibiotics and perhaps certain species of bacteria, notably staphylococcus. Notable among the antibiotics which may give rise to increased resistance during treatment are streptomycin, erythromycin and of the more recent ones, novobiocin. Also, penicillin may increase the resistance of certain staphylococci *in vivo* under suitable conditions. The use of combinations of antibacterial agents, such as those that have been so successfully employed in the treatment of tuberculosis, may delay and depress but not entirely prevent these effects. However, the infecting organism must be susceptible to each of the agents used in the combination at the start of treatment if any beneficial effect is to be obtained.

There is still a need for new agents or new methods of treatment to combat many important infections, even among those caused by some of the most common pathogenic bacteria against which our present armamentarium is still inadequate.

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Influenza: History, Epidemiology and Current Problems[1]

By JOHN J. HANLON, M.D., M.P.H.[2]

HISTORY

WITH influenza we are dealing with one of the oldest known, most elusive and most common infections of man. How far back into antiquity it goes is not known. There are indications that Imhotep was familiar with it and that it occurred in epidemic form in Egypt of the Pharaohs.

Since the early 16th century, epidemics and pandemics have been described and documented in the Western World under a wide variety of names, usually designating some nation or people—other than those of the describer. Hence we read of the English sweat, the Gallic malady, the Hungarian sickness, the Dunkirk rant, the British pest, the Spanish flu, and now Asian influenza.

Its more common designation apparently goes back to the late middle ages when Italian astrologers and physicians presumed it to be influenced by stars and comets . . . hence the name *influenza*. Other causes to which outbreaks were attributed have been volcanic eruptions, meteors, the aurora borealis, excessive atmospheric ozone, insect scourges, severe climatic changes, vegetable germs and the Pfeiffer bacillus. More recently, Smith, Andrewes and Laidlaw (1) in England in 1933 isolated a filterable virus from throat washings of a patient and demonstrated beyond doubt that it could give rise to the clinical syndrome in otherwise healthy adults. This provided at least a comforting, albeit temporary, etiologic base from which to work. However, the next few years brought to light a number of variants or mutants of the parent strain. The confusion was resolved by referring to all of these viruses as type A in anticipation of subsequent discovery of additional main types. This became reality in 1940 when Francis (2) and Magill (3) in this country independently isolated a similar but antigenically distinct virus with its own related variants or mutants. These were collectively referred to as type B. Subsequently, two other antigenically distinct types, C and D which show no cross-immunity, have been isolated. These each appear to be homogenous, with no sub-type variation.

A significant investigative step was made by Smith, Andrewes and Laidlaw (1) when the virus was found to be capable of infecting ferrets; later work showed that mice and fertile chicken eggs could also be infected. This latter was followed promptly by the observation by several investigators (4, 5) that the virus had the ability to agglutinate the red blood cells of several animals and of the developing chick embryo. This formed the basis for a relatively simple diagnostic test (6) in that a strain-specific antibody will inhibit the agglutination of erythrocytes by a virus of the homologous strain. Also this same principle makes possible the diagnosis of influenza "A" or "B" by demonstrating a rise during convalescence of the antibody titer to one type of virus but not to the other.

COURSE

Whatever the particular causative strain of virus, suffice it to say that they all give rise, with varying degrees of clinical severity, essentially to the same series of signs and symptoms —a brief incubation period of 1–3 days, the sudden onset of headaches, chilliness, general fatigue and achiness, especially in the muscles

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of the back and the extremities. A sensation of ocular burning or pain is a not uncommon symptom. A spiking temperature rise occurs, sometimes going as high as 103–104 F. Usually an irritating hacking cough develops which may become mildly productive. Symptoms and temperature generally parallel each other and usually last for 3 to 5 days. Occasionally there may be signs and symptoms related to the gastro-intestinal tract such as anorexia, nausea and occasional vomiting, but not diarrhea. The respiratory symptoms may proceed to a rhinitis, tracheobronchitis, laryngitis, and in severely complicated cases to a pneumonia which tends to be fulminating. A striking characteristic of the usual case is prostration, fever, and symptoms all out of proportion to the physical and laboratory findings. The throat may appear normal and the lung fields clear except perhaps for a few transitory crackling rales. In uncomplicated cases, the pulse and respiratory rates remain normal and the blood picture does not change significantly.

Most all of these complications have been found to be due to secondary invaders, or as some have referred to them, "bacterial hitchhikers", some of which may have been picked up at about the same time as the virus. Predominant among the bacterial invaders are streptococci, pneumococci, staphylococci and H. influenzae. Of these, at the present time, the staphylococcus presents the most difficult problem in view of the recent development of strains resistant to antibacterial chemicals and antibiotics.

EPIDEMIOLOGY

Influenza is classified as an airborne droplet infection of the upper respiratory tract. It may also be spread by direct contact and by soiled fomites. As such, it passes from person to person, and all individuals previously uninfected by the specific current strain are presumed to be susceptible. From the standpoint of group spread, without going into details, its quantum behavior is determined essentially by the ratio of susceptibles to immunes on the one hand, and rates and types of epidemiologically effective contacts on the other. Many diverse factors condition the latter, including housing and overcrowding, cultural behavior, and climate, especially as it relates to preceding or concurrent mild upper respiratory illnesses such as colds and pollinosis. Obviously this is very much an over-simplification, not only in terms of existing knowledge but more significantly in terms of certain fundamental gaps in our knowledge, especially with regard to the inter-epidemic behavior of both the virus and the host.

Generally speaking, it would appear that the virus smolders in a population causing a constant minimal incidence of illness breaking through in epidemic or even pandemic form on a more or less cyclic basis, either because of epidemiological reactivation or by virtue of the development of a new mutant against which mass resistance is non-existent.

America was apparently first affected in 1758 by an epidemic of typically high morbidity and low mortality. A more extensive outbreak of similarly low severity affected Europe and Asia in 1782. While a number of other outbreaks since have merited documentation, the pandemics of 1889–90 and of 1918–19 are by far the most notable. This is especially true of the latter—which has been referred to as one of the greatest, if not the greatest, single catastrophe which ever affected the human race.

It may be of interest briefly to review this holocaust which affected 20,000,000 people in the United States alone and caused 850,000 deaths among them.

A mild type of influenza was recognized to exist in epidemic form in several parts of the United States during 1916. Late in the following year and early in 1918 it broke out again in a number of Army camps but was still clinically mild. By spring of 1918 it had spread to the civilian population and mortality from pneumonia was noted to be rising significantly. Meanwhile, similar epidemics were building up in Europe and elsewhere throughout the world. Late in August it appeared suddenly in severe form in Boston, Massachusetts and in Camp

Shelby, Mississippi and rapidly spread from these localities along the Eastern Seaboard and the Gulf States and thence westward to eventually blanket the entire country. The rapidity of spread is indicated by the brief interval of one month between the epidemic peaks in Boston and in San Francisco. Incidentally, the peak of death tended to follow the onset of the epidemic in a given locality by about one month. Mortality was highest in young adults —in contrast with prior and subsequent epidemics which have tended to affect worst the very young or the very old. Early in 1919 came a recrudescence of the disease especially in those places least affected in the preceding fall. In summary, the experience was a mild phase in the spring of 1918, an explosive rapidly spreading epidemic of high mortality in the fall of 1918, and a recrudescence or "mop up" phase in the early part of 1919.

CURRENT OUTBREAK

The first the western world heard about the current outbreak was when it broke out in startling proportions in Hong Kong, affecting an estimated 250,000 persons in that city. However, an American scientist who since visited the Soviet Union as a member of an exchange group of scientists was told that during the winter of 1956–57 an influenza epidemic occurred in Vladivostok. Apparently, from there it was carried to various parts of the Soviet Union and outbreaks occurred last spring in Moscow and several other places in the USSR. Presumably, this was the same disease. In fact, a sample of a live virus vaccine has been received in this country from the Soviet Union and the strain isolated from it appears to be identical with the other strains of Asian virus obtained elsewhere. Subsequently, it was learned that outbreaks had occurred in Shanghai, Peking, and other cities in Red China.

After hitting Hong Kong, it spread rapidly throughout the Far East, across South Asia, the Middle East, and since has appeared in several places in Europe, including the Netherlands. Since then, it has appeared in epidemic proportions in several places in Europe, Greenland, Alaska, in large areas of Latin America and in the United States. It entered the United States through a number of points on both coasts, but most significantly, through California. The first confirmed case in the U. S. A. was reported from Cleveland, Ohio, on July 12, 1957 in a hospital orderly recently returned from Japan. Several days earlier, however, the first suspected case in Pennsylvania was reported near Scranton, again in a young man just returned from Japan. This was subsequently confirmed by the laboratory as caused by the Asian Flu virus.

Meanwhile, a number of cases and small epidemics of this disease occurred widely spread throughout the country. A number of Army camps in California and others elsewhere have been affected. At the end of June, enough cases occurred at the national meeting of the Westminster Fellowship at Grinnell, Iowa, to cause the meeting to close before schedule. It is significant that of the first 12 cases, 11 were in young people from California and the 12th in a Nevadan who accompanied the Californian group. Subsequent to departure home from Grinnell, cases have been reported among delegates in many places throughout the United States. Of particular interest to Philadelphia has been the isolation of Asian Flu virus from some of the boys who were ill during the International Boy Scout Jamboree at Valley Forge.

PROBLEMS

The present situation confronts us with a number of interesting problems and puzzles, as well as with an opportunity perhaps to obtain answers to some of them. First of all, this is the first time in history that a large population has found itself in the path of an imminent epidemic with the viral strain identified, isolated, and a reasonably effective vaccine produced, and in the process of fairly wide administration. The circumstances of these scientific and industrial achievements has been nothing short of spectacular in terms of the various time factors involved. Beyond this, our population is generally healthy, well-nourished,

and well-housed. Also, we are exceptionally well supplied with medical and allied personnel, health facilities and pharmaceuticals with which to combat possible complications. The question arises, what will be the effect of this upon the morbidity and mortality as well as upon the smooth continuance of essential community services?

Another intriguing problem is presented by the discovery of antibodies in elderly individuals in Germany and in Massachusetts who were involved in the 1889–90 epidemic. What is the significance of this? It could indicate that viral strains may in actuality lie more or less dormant (in an epidemiological sense) for long periods of time and then become active again, in contradistinction to the concept of new mutants developing. If this were so, then two possibilities might be considered. On the one hand, the eventual development of a truly universal influenzal vaccine comes close to reality. On the other hand, there would be cause to be concerned about the possible return or recrudescence of the 1918–19 strain sometime in the future.

Among the groups seriously affected, especially in 1918–19, were pregnant women. Unfortunately, at that time there was no reason to consider effects on the fetus and child other than illness or death. Since then, there has appeared reason to look for possible relationships between viral infections during pregnancy and the development of certain congenital anomalies in the developing child. This has been done with some diseases, notably rubella, and now studies are underway with regard to the present strain of influenza virus.

Mention was made of the armamentarium of antibacterials available to us. While this gives some cause for satisfaction and comfort, the question may be raised of the problem of an increasing number of drug and antibiotic resistant strains of possible complicating bacteria as one result of the promiscuous use of these materials. In this situation, however, the case fatality rate is so low that it may not be possible to study this question adequately.

These, then, are a few of the highlights relating to this disease of current interest and a few of the many questions which it poses. One thing, I believe, is unquestionably true. Out of this present experience, the medical profession and the world at large is certain to emerge with far more knowledge of this hardy pathological perennial—influenza.

Acknowledgment

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The American Heart Association's Albert Lasker Award

For Distinguished Achievement in the Field of Cardiovascular Research 1957 to

Isaac Starr, M.D.

THE 1957 Albert Lasker Award of the American Heart Association is presented to Isaac Starr, from whose creative mind and persistent endeavors have come numerous fundamental contributions to our knowledge of the heart and the circulation.

Dr. Starr excels as physiologist, pharmacologist, clinician, research scientist and teacher. Above all, he has won renown as that rare individual, the independent thinker. Rejecting the circumscriptions of conventional ideas based upon incomplete knowledge, he turns upon each unsolved problem the penetrating light of original thought.

This bold approach is well illustrated by his historic work in elucidating the mechanisms of congestive failure. Through laboratory experiments which are a model of scientific reasoning, planning and execution, he led in sweeping away concepts complacently accepted for a century. His work stimulated a tremendous volume of research by others, research that has tended to confirm the ideas he so brilliantly conceived and first tested. To Dr. Starr and to those who followed in the paths he indicated, we owe today's vastly greater insight into the fundamental physiology of congestive heart failure—an insight now at the service of medicine in helping all those afflicted with this condition.

Another example of Dr. Starr's pioneering may be found in his development of the first practical ballistocardiograph. While others preceded him in this effort, it was not until Dr. Starr devised his apparatus in the 1930's that a successful method was achieved for recording the mechanical thrust of the heart.

Among his many other achievements may be cited his contributions to scientific knowledge of renal physiology and of the treatment of peripheral vascular disease. Furthermore, his great interest in drug reactions in man is reflected not only in his many publications in the field of pharmacology but also in his 20 years of service on the Revision Committee of the U.S. Pharmacopoeia. He supplemented his own immense knowledge in this field by having all his students, as he had himself, experience through self-medication the effects of all the common agents used in the treatment of patients.

He is revered as colleague and teacher by those who have known him during his long and distinguished career at the University of Pennsylvania School of Medicine, which he has served for 35 years in many capacities —ranging from instructor to dean, and where he now holds the title of Hartzell Research Professor of Therapeutics. Among his colleagues he is greatly admired for the persistence with which he has followed his patients for many years with repeated examinations, thus greatly enhancing our knowledge of various prognostic signs of value in cardiac patients.

To a man of original and brilliant mind, of gentle and understanding nature, of enduring accomplishment, to Dr. Isaac Starr, the American Heart Association is proud indeed to present the Albert Lasker Award for

Dr. Isaac Starr, of Philadelphia, receives the Albert Lasker Award of the American Heart Association for distinguished achievement in the field of cardiovascular research. The Award was conferred by Dr. Robert W. Wilkins, of Boston, President-Elect of the American Heart Association at the Association's Scientific Session (October 27, 1957) in the Hotel Sherman, Chicago, Illinois. Dr. Starr, Research Professor of Therapeutics, University of Pennsylvania Medical School, was cited primarily for a series of bold laboratory experiments which determined the mechanisms of congestive heart failure. The award, one of the highest honors in American medicine, consists of a gold statuette of the Winged Victory of Samothrace, an illuminated scroll and an honorarium of $2,500.

Distinguished Achievement in the field of cardiovascular research.

E. V. Allen, M.D.
President, The American Heart Association.

K. Kohlstaedt
Chairman, The Lasker Award Committee of The American Heart Association.

DR. STARR'S RESPONSE

To be honored as you have honored me I find embarrassing, but after my embarrassment has been overcome—nay rather brought under control—I am led to reflect on the combination of circumstances which has permitted me to be so fortunate.

Of my many good teachers, two have been great ones. It was Professor E. G. Conklin of Princeton who first aroused my interest in the biological sciences and to the challenge of the big rather than the small problem. To Professor A. N. Richards of the University of Pennsylvania, to whose laboratory I came planning to spend a year or two, and stayed for ten years, I owe far more than technical

training, though rigorous discipline in physiological and biochemical methods was not lacking. The spirit of his laboratory had something inspiring about it. Not by word of mouth, but by example, were we taught that the road to exact information is long and difficult and requires not only skill, patience and fortitude, but also agonizing work. What wonder that young men of vision were challenged; it is doubtful if anyone in America attracted a more brilliant group. To work among such people was training in itself.

The training period over, I became in lasting debt to the Rockefeller Foundation for support, through a grant to Dr. Richards, during five very critical years; and then to my old teacher of Dermatology, Professor Hartzell, who endowed the chair which I still occupy. Nor can I discuss financial matters without a tribute to my wife who has always understood and appreciated intellectual effort and, most fortunately for me, has never exhibited the slightest interest in mink coats or Cadillacs.

I have been most fortunate in another respect which has been a powerful factor in what success I have had. We have been living in a period when the spirit of the times has been increasingly propitious for research; a time when the old ideas are being questioned and re-evaluated, and when new ideas receive a ready hearing. I doubt if there has been a like period since the Renaissance.

Research has long had the support of those of the rich and powerful who, with unusual insight and discrimination, have disinterestedly concerned themselves with the betterment of mankind; and I must pause to extend my thanks to the distinguished family who have endowed the rich award that I have just received. But now-a-days, in addition to the gifts of great benefactors, research draws both understanding and support from the people as a whole as never before, and from their agent the government. And so let me pause once more and record my thanks to the thousands of people who, by their great interest and many contributions, have enabled our American Heart Association to raise large sums for the furtherance of research, a feat which, at the onset of my career, would have been regarded as utterly beyond the realm of possibility. And let me finally convey my thanks to that agency of the people, our government, which, acting through the U.S. Public Health Service, has so long and so adequately supported my research.

There is little doubt that the advance in the practice of medicine which has taken place in my medical lifetime exceeds that of the preceding five-hundred years. What a time to be alive and interested in such things! But, though I am the one who is honored, you, ladies and gentlemen, have also been playing a part in this advance. In research as in other matters, "no one liveth to himself alone." The credit for the great medical accomplishment of our generation belongs not to doctors alone, for all types of human knowledge have been drawn upon and the roots spread far. Support for research, both moral and financial, stems no longer from the few but from the many. Therefore, while you have seen fit to honor me today for playing a small part, you, ladies and gentlemen, of both the medical professon and of the laity, also deserve your share both of the honor and of the satisfaction which is the just due of those who have worked to facilitate this medical advance, surely one of the great achievements of our era.

Though the honors go to the few, the medical advance depends on the many. As my old teacher Professor Conklin so wisely used to say, "new things are not discovered, they grow." This is a profound truth. Though you may note that I carefully avoided any mention of these wise words until I had the award in my pocket, they will always be before me when I think of the great honor you have done me today.

Dr. Frank N. Wilson: A Biographical Sketch[1]

By THOMAS M. DURANT, M.D.[2]

DR. FRANK NORMAN WILSON was a genius. This is a fact that would be affirmed by all of the large number of men who studied under him, and by all those who know his work well (1). His genius, however, was not of a spectacular type. He probably would not have been chosen by Paul DeKruif for a story in a popular journal. Nevertheless he was gifted with mental acuity possessed by few mortals, and the magnitude of his contribution to the welfare of humanity can be readily compared to that of modern surgeons who have developed techniques for correcting heart defects. It might even be said that his contribution was greater than these in some respects, since Nature is particularly reluctant to yield her *basic* secrets: for example, those relating to the electrophysiology of the heart. It was secrets involved in the latter topic that intrigued Dr. Wilson and led him to devote his entire career to an attempt at their elucidation. As will be brought out later, the dedication of his genius in this direction was rewarded with great success.

Born on a farm in southeastern Michigan, Dr. Wilson had the good fortune in his early rural school days to have an able teacher who evidently recognized him as an unusual pupil and did much to provide him with motivation and to develop his aptitude for the biological sciences. We may be justified, perhaps, in comparing this man, William Sackett, with James Bovell, whose influence on the young William Osler played such an important role in the development of the man who became the great Sir William. For all of us who are teachers there is much to be learned from this example. There can be no denying the fact that our responsibility in dealing with the young entrusted to us is great, particularly since one of these may be a future Osler or Wilson. No doubt the genius in them would make itself evident no matter what we do. How much happier we would be, however, to feel that we fostered rather than inhibited the flowering of such talent. We cannot allow ourselves to accede to the present American tendency favoring mediocrity in education, since we will then move toward a loss of all future "satellite" races, astronomical or otherwise, and Our Star may no longer be in ascendency among the world of nations.

Dr. Wilson, himself, did not know why he chose medicine as a career. I presume this is true of many, and it is, no doubt, the unconscious influences that dominate. I would suspect that Sackett's role in this may have been a very considerable one. Those who knew him well, however, are agreed that Dr. Wilson could have made an equally great contribution in other fields had his choice been different. What Samuel Johnson had to say is probably quite apropos: "The true genius is a mind of large general powers, accidentally determined to some particular direction." It is probably quite safe to say, at least, that, had Wilson chosen mathematics, his contributions would have been great in that field also.

Following graduation from the University of Michigan Medical School in 1913, Dr. Wilson accepted a position in the department of medicine under Dr. A. Walter Hewlett. This was at a time when the electrocardiograph was just becoming known in this country. Under the influence of Sir Thomas Lewis, pupil of Sir James Mackenzie, this instrument of Einthoven's design had become recognized as the best means of diagnosing the arrhyth-

[1] Presented before the Section on Medical History, College of Physicians of Philadelphia, 15 October 1957.

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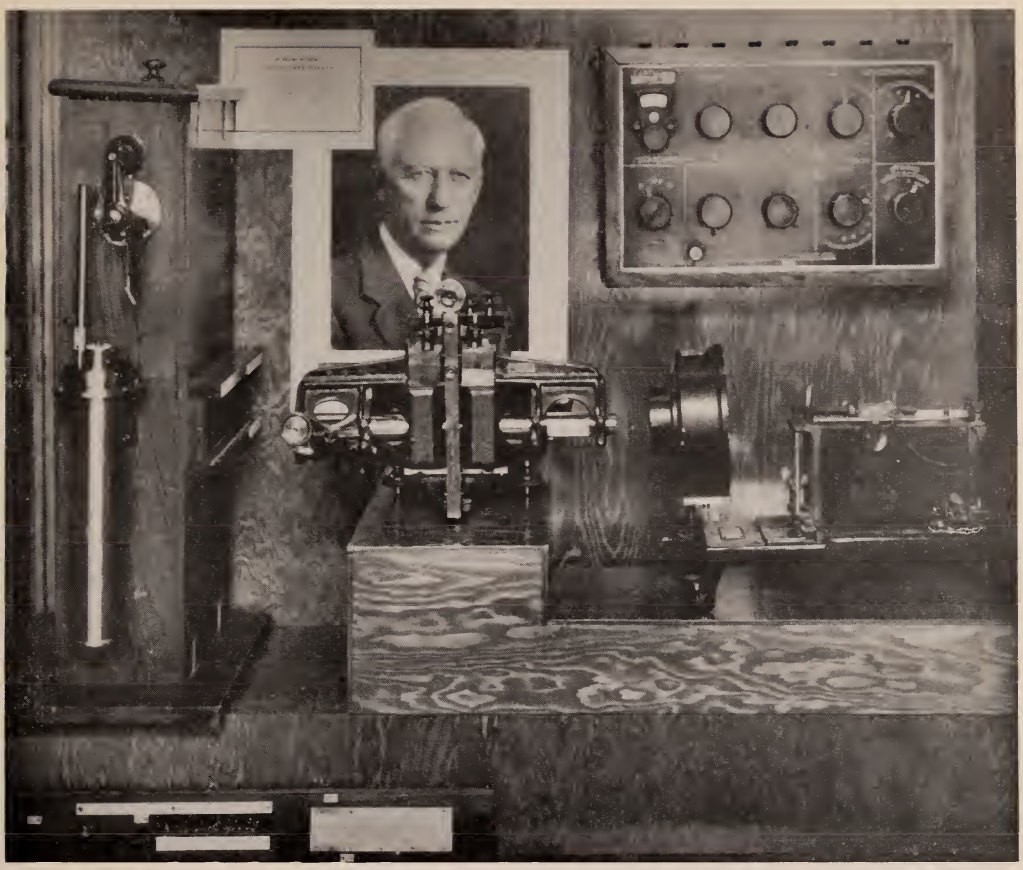

FIG. 1. Exhibit in Division of Medical Sciences, Smithsonian Institution, Washington, D. C. The string galvanometer in the center of the photograph, which was manufactured by the Cambridge Scientific Apparatus Company, was purchased by Dr. Wilson in 1919; the Cambridge camera on the left and the Hindle-Williams control box in the upper right, above the carbon arc light, were obtained by him in the early nineteen-twenties.

Photograph, courtesy of Dr. John B. Blake, Associate Curator, Division of Medical Sciences, Smithsonian Institution, Washington 25, D. C.

mias, and definitely superior to Mackenzie's polygraph. Despite this, however, there were only about twelve of these instruments in the entire United States and these were cumbersome, expensive devices. It is to Dr. Hewlett's great credit that he assigned Dr. Wilson the job of assembling and using the first instrument obtained by the University of Michigan in 1914. Whether his selection was fortuitous or not, I do not know, but I would like to think that he saw in the young Wilson the kind of talent that would utilize the new diagnostic tool in an exceptional manner. At any rate, the forces moulding Dr. Wilson's career were at work and we owe a debt of gratitude to Dr. Hewlett for his choice. Knowing Dr. Wilson as I did, I can well imagine how intrigued he became with the machine assigned to him, and his dedication to a lifetime of study of its potentialities was undoubtedly nearly complete even at this early date.

The year 1914 was marked by another event which was to have a very important bearing on the career of Dr. Wilson. This was his marriage to Miss Juel Mahoney, a student in the University of Michigan School of Music. In selecting his bride he had chosen well, for she became one of the very important factors in his life work. If ever a wife lived up to the title of "Helpmeet," Mrs. Wilson was that one.

She knew that she had married a man destined to accomplish great things, and she devoted her life to him in such a manner as to make readily possible his dedication to the task he had chosen. She removed from his shoulders every possible burden of ordinary living. She was his companion when needed, but when he was deep in mental concentration (as was very often the case) he was undisturbed. The world of electrocardiography owes a great debt to this fine woman.

Few careers, even of the great, proceed uninterruptedly toward their successes or triumphs. The first interruption of significance in Dr. Wilson's career came with the entrance of the United States into World War I. In 1917 a group of cardiologists from this country was chosen to work with Thomas Lewis at Colchester, England. Dr. Wilson was the youngest of the group selected. Though there was thus created a hiatus in his career, it turned out to be a cloud with a silver lining. It was during his stay in Colchester that Drs. Lewis and Wilson became fast friends, and this was a friendship that continued to Sir Thomas' death. Dr. Lewis recognized the genius in the young man working with him and he was later instrumental, along with Einthoven, in encouraging Dr. Wilson to continue his career at a time when he was dejectedly ready to abandon it. It was also at Colchester that other important lifelong friendships were established, one of especial importance being that with Dr. Samuel A. Levine. Later these two enjoyed rooming together each year at the annual Atlantic City meetings of the Association of American Physicians and the Society for Clinical Investigation. Each admired the other greatly and profited immeasurably from their comradeship.

Following the war Dr. Wilson returned to the United States and worked for a while at Washington University in Saint Louis. It was here that he first worked with Dr. George R. Herrmann, and an important study was done by them on the subject of bundle branch block. Included were some fundamental observations concerning the electrical field as it is produced by the heart within the body as a volume conductor. These observations were to have an important influence on Wilson's later work. His devoted dedication to electrocardiography was quite evident in these early days and has been well described in an article written about him in later years by Dr. Herrmann (2).

In 1920 Dr. Wilson returned to Ann Arbor, having been promised a fine heart station in a projected new hospital building. Unfortunately, however, five years were to elapse before the new buidling was to become a reality. The intervening years were enough to try the soul of any man, especially one burning with a desire to know more of Nature's secrets as displayed in the electrocardiogram. The equipment that was available was not worthy of the genius who was to use it, and the only location that could be found for a heart station was a hollowed-out room under the stairs in the medical wing of the old hospital building. Here, with the discordant accompaniment of shuffling student feet overhead, and with dust drifting down on his instruments, our dedicated genius proceeded to do tedious but excellent work, and contributed many important articles to medical literature. Illustrative of the attitude displayed toward Dr. Wilson at this time is a remark Dr. Wishart relays to us. He says his chief of those days was often referred to as "that eccentric who plays with impractical gadgets in the hole under the stairs."

During these years there was one investigation of Wilson's which deserves particular comment. This had to do with the repolarization process in the heart. He had discovered that the form of the T wave of the electrocardiogram of normal persons could be considerably influenced by the drinking of iced water. This was only the first of other important observations concerning the T wave, but it had a profound influence on Dr. Wilson's interpretation of electrocardiograms, an influence which can well serve as a lesson for many of us today. Realizing the potential lability of the final portion of the ventricular

complex, he was never willing to make the diagnosis of myocardial disease when nonspecific types of T-wave change were observed. He referred to these as simply representing "myocardial changes." Our present knowledge of electrolytes and their effect on the electrocardiogram, as well as the influence of tonus of the sympathetic nervous system, have fully supported his conservative position in this matter. It should be noted, in passing, that over-diagnosis of electrocardiographic findings can have even more devastating effects on the life of a patient than can underdiagnosis.

When the new hospital was completed finally in 1925, Dr. Wilson at last had a spacious heart station in which to work. Two years later, in 1927, he also obtained a magnificent double string galvanometer which had been built in Einthoven's laboratory at Leyden. This machine was designed to work with unusually great string tension and provided a means, of course, of comparing time relationships in two leads taken simultaneously. It was to serve him well during the years when he made his greatest contributions. It was in 1927 that Dr. C. C. Sturgis came to Ann Arbor as Professor of Medicine. This fine leader was completely aware of the research potentialities which were in Wilson, and made full provision for him to be relieved of all academic responsibilities. His new freedom to work as he pleased was to become a particular boon a few years later.

Meanwhile a prolonged illness prevented any immediate important effect. This constituted a second hiatus in his career. As was true of the first hiatus, however, this one was also to have its beneficial aspects, for during his long convalescence Dr. Wilson made a very thorough study of mathematics. He had long felt that no one could ever hope to understand the phenomena observed in electrocardiography without utilizing this basic discipline. Dr. Samuel Levine speaks of his having "plunged into this study with youthful vigor," and adds "Few men in medicine would have made such an attempt and fewer still would have been successful" (3). It is quite safe to say that much of the success of his later research was possible only because of his proficiency in this field. His mastery of it was so complete as often to make possible in advance the correct calculation of what was to be expected in the investigation of a particular biological phenomenon. I marvel at the triumph Dr. Wilson achieved in this, but I would like to emphasize that it is a representation not only of his genius, but of his absolute dedication to the subject which had become his life work.

Another byproduct of the illness was Dr. Wilson's realization that he needed a place where he could be at peace with the world of nature and so concentrate on the problems which were puzzling him. As a result he bought a farm at Stockbridge, Michigan, and at this delightful spot he obtained frequent refreshment of mind and body throughout the remainder of his life. No doubt many of the ideas which led to later successful experiments had their origin here rather than in the midst of his busy laboratory. Here, too, he was able to pursue his hobby of bird photography, a form of recreation he had first learned from Sir Thomas Lewis. No man, no matter how great his genius, should deny himself the opportunity to withdraw at intervals from the whirl of life's events, nor should he be without a relaxing substitute for his usual occupation.

Toward the end of his long illness, in the year 1929, there was admitted to the University of Michigan Hospital a case destined to have a very considerable bearing on Dr. Wilson's work for the next few years. This patient of Dr. Paul Barker's had purulent pericardial disease requiring surgery, and the exposure of the heart effected by the late Dr. John Alexander permitted electrocardiographic studies never before performed in the human. When the surface of the exposed heart was stimulated electrically by Drs. Barker and Macleod, complexes were produced of a type not in keeping with the then generally accepted concept of bundle branch block. Developed by Sir Thomas Lewis, this concept

had been based on experimentally produced lesions in dogs. What we now know to be *left* bundle branch block was then called *right*, and some of the instances of what we now know to be *right* were then labelled *left* bundle branch block. Lewis' concept had been challenged by Drs. Oppenheimer and Pardee in 1920 as a result of pathological findings in human cases, and Dr. Fahr had objected also on theoretical grounds. Until that time, however, Dr. Wilson had gone along with the accepted teaching and there had been many a friendly argument with Dr. Oppenheimer concerning it. During one of these arguments the latter had remarked, somewhat sarcastically, Dr. Wilson tells us, that it would be necessary to cut one of the bundle branches in the human to convince Dr. Wilson that the classical teaching was false. Wilson had replied that he would accept the opposite view if stimulation of the exposed right ventricle produced diphasic complexes of the kind Dr. Oppenheimer attributed to left bundle branch block. Thus Dr. Barker's case provided the conditions Dr. Wilson had asked for, and it appeared that the classical theory was, indeed, wrong. His interest in the findings was great, and his return to the laboratory in that same year was marked by a burning desire to test further the new concept.

The years from 1929 to 1940 were perhaps the most productive in Dr. Wilson's career. Fortified with profound knowledge of the mathematical sciences, and intrigued by a new concept of bundle branch block, he set out to study afresh the phenomena involved in ventricular excitation. Needed for these studies was a direct lead for animal use and a semidirect, precordial lead for use in humans that would be as nearly unipolar as possible. Dr. Wilson had used precordial leads in his laboratory in a desultory way ever since 1919, but never before had they been as systemically studied as at this time. The placing of one electrode on the precordium and the other on the leg made it possible to consider the former as an "exploring" electrode and the latter as an essentially "indifferent" one. The electrode connected to the leg did often have potential of more than negligible magnitude despite its distance from the heart, however, and a better means of obtaining unipolar electrocardiograms was required. To meet this need mathematical knowledge plus "hunches" (which appear to rise spontaneously in the mind of the genius, but which are undoubtedly determined by unconscious thought processes) led to the development of the central terminal. This device utilized an indifferent electrode connected to each of the three extremity leads through resistances of 5000 ohms. Dr. Wilson and his associates carried out experiments of many kinds to demonstrate that the potentials of this terminal were of insignificant magnitude, and that the precordial electrode could, therefore, be considered a unipolar lead. This method of taking precordial leads has been universally adopted and has become part of the connections of all commercial apparatus available today.

Using unipolar electrocardiography Dr. Wilson and his associates soon established beyond a doubt the fact that the Lewis concept of what was right and what left bundle branch block was reversed, and it was not long before Sir Thomas, himself, admitted that he had been wrong. Further study showed that there were various subtypes of what had been formerly called "the common type" of bundle branch block, and, when a proper sorting of types according to right or left involvement was accomplished, a marked difference in the frequency of the two types no longer existed. The terms *common* and *rare* type of bundle branch block thus had to be discarded. One form of right bundle branch block well known today and characterized by a broad S wave in lead I, was first described as such by Dr. Wilson and associates, and in Europe today it is often called the "Wilson" type of bundle branch block.

Among many other investigations carried out in the following years there was an especially important series relating to myocardial infarction. This led to further systematic elucidation of the phenomena of normal and

abnormal ventricular excitation. Much of what we now know concerning endocardial potentials, the intrinsic deflection, and the Q waves has been derived from this research. Dr. Wilson's concepts also made possible a correlation of the findings in precordial leads with those of the extremity potentials and standard leads, and his ideas relating to the electrical position of the heart have become very useful in understanding many electrocardiographic phenomena. As a result, today's student of electrocardiography does not have to memorize patterns nor does he have to make diagnoses in an empirical manner as was formerly the case. There are sound principles upon which to place reliance, and we have Dr. Wilson and the many men who worked with him to thank for establishing these principles and for laying down much of the foundation upon which the modern science of electrocardiography stands.

Froude, in writing about Thomas Carlyle, has wisely said, "High original genius is always ridiculed on its first appearance; most of all by those who have won themselves the highest reputation in working on established lines. Genius only commands recognition when it has created the taste which is to appreciate it." These words could be applied with equal force in the case of Frank Wilson. Year after year he presented the latest developments in his research to the savants of Internal Medicine at their important Atlantic City meetings and, year after year, most of the audience walked out when he began to speak. Generally only a faithful few remained to hear papers that have since become generally recognized as classics. Only after the lapse of a good many years, and much discouragement for Wilson, did it begin to dawn upon the majority that they would have to expend the effort necessary to understand Wilson's precepts if they were to be most effective in electrocardiographic diagnosis. Little by little the taste for the genius' work was created, his audiences grew in size, and his fame became worldwide.

It is good to know that fame and recognition did finally come to one who so richly deserved them, and that this happened while he was still alive to appreciate it. It is entirely possible, however, that this was not for the best in one sense at least. In his later years, Wilson was so busy with consultations and with visiting physicians from near and far desiring postgraduate training that there was a definite slackening in the appearance of new concepts from his laboratory. It is quite possible, however, that the inspiration the Wilson genius gave to those who were fortunate enough to have close contact with him more than compensated for any loss suffered due to a lessening of his research. Many of the students motivated by Wilson have been carrying on in subsequent years and have added materially to the foundations laid by him.

The last long paper to appear from Wilson's laboratory, "On the Possibility of Constructing an Einthoven Triangle for a Given Subject," was based on work done at the same time that a Dutch physicist and physician, Burger and van Milann, did their important work constructing triangles representating the electrical, as opposed to the anatomical, differences that obtain from one individual to another. With these studies there has been initiated another chapter in electrocardiographic research destined probably to provide new leads and new methods even more accurate than those using the central terminal. It is of interest to point out that present advances along these lines are largely dependent upon men who are either biophysicists or electrical engineers (Schmitt, Frank, McFee, Nelson, Johnston, etc.). This is in keeping with Wilson's early recognition that physicians could not solve the really basic problems of electrocardiography without aid from the fundamental sciences. As in other lines of modern research it is the communion of many disciplines that extends the frontiers of our knowledge.

Illness once again began to play a part in Dr. Wilson's career toward its close. He had begun to have symptoms of coronary heart disease as early as 1943, but it was not this that influenced his activity seriously. It was only when he was stricken with tuberculosis in 1948 that he was forced to give up active

participation in postgraduate teaching and other work. This infection was unresponsive to treatment and, combined with the effects of coronary disease, led to his death in 1952.

Thus, there passed from the scene a man possessed of a great mind and a rare genius. He has been the inaugurator of the modern era of electrocardiography, and all of us who practise medicine and a vast number of our patients are immeasurably indebted to him for the contributions he has made to medical science and to the welfare of mankind. Also, as Dr. Samuel Levine has said (3), there are few men who have had "so many devoted friends, colleagues and inspired students all over the world," as has Frank Norman Wilson.

Acknowledgement: The author is indebted for the information in this paper not only to the personal contact he was privileged to enjoy with Dr. Wilson, but also to the volume edited by Drs. Johnston and Lepeschkin listed as reference number (1). The latter is highly recommended to all persons interested in electrocardiography, and the footnotes of the editors provide valuable comments concerning Dr. Wilson's life and work.

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Leonardo da Vinci and Andreas Vesalius: A Comparison[1]

By MARSHALL SMITH, M.D.[2]

SINCE the publication of "De Humani Corporis Fabrica" in 1543, its author, Andreas Vesalius, has been considered the father of modern anatomy. Prior to his time all anatomy was taught from the works of ancient Arab and Greek authors, particularly Galen and Avicenna. No other anatomist of Vesalius' era was known to have been as observant and as inquisitive concerning the human body, and certainly Vesalius was the first to suggest the teaching of anatomy by means of accurate drawings made from carefully performed dissections.

This position went unchallenged for over 300 years. Then in 1898 and 1901 Sabachnikoff in Paris published a transcription of the anatomical works of Leonardo da Vinci compiled by Piumati. A third collection, in six volumes, was published in 1911–1916 by Vangensten, Fonahn, and Hopstock in Christiania (1). The originals from which these facsimiles were compiled are to be found at the Royal Library at Windsor, Berkshire, England. Following the publication of Piumati's work, Jackschath (2) wrote an article in which he attempted to prove that Leonardo had written a major treatise on anatomy, of which the available drawings were a part, and that Vesalius had plagiarized from da Vinci in the "Fabrica." His arguments were based primarily on Vesalius' young age (29 years) and certain similarities between the drawings in the "Fabrica" and the available works of Leonardo. Other anatomists, mostly German, soon came to Vesalius' defense and succeeded in upholding Versalius' position as author of the "Fabrica."

At the time of the argument, which was started by Jackschath in 1902 and lasted until about 1916, most articles which were written displayed a strongly biased point of view. In the literature of the time there was no article written, at least in English, giving a comparison of the works of the two men in a fair, unbiased manner. In recent years much has been written about each man individually, but as yet the English literature contains no true comparison. It is the purpose of this paper to make up for this deficit in our historical literature.

BIOGRAPHIES

Before considering the works of Vesalius and Leonardo a short biographical sketch of each man is in order. This will help in better understanding the motives of each in doing the drawings and will enable judgment of the quality of the drawings to be based somewhat on the material available to the artist.

Leonardo da Vinci was born in the Tuscan hill-town of Vinci on April 15, 1452, the son of a young notary, Ser Piero, and a nearby village girl, Caterina. In spite of his illegitimate birth he was accepted into the family of his father. Leonardo's father married a woman of his own station that same year, and the young boy was raised in a normal family environment. Little is known of his childhood except that he spent much time in outdoor physical activities. His education was of the simplest sort, primarily mathematics. He was never educated in the classical languages, although he did learn some Latin on his own.

Early in his life Leonardo displayed an in-

[1] Edward Bell Krumbhaar Prize Essay I, Section on Medical History, College of Physicians of Philadelphia, 12 February 1957.

[2] Resident in Medicine, Hartford Hospital, Hartford 15, Connecticut.

terest in drawing and observing nature. He had few youthful companions, later commenting "If you are alone you belong entirely to yourself" (3a). Leonardo's father was apparently quite sympathetic with his son's artistic leanings and showed some of his works to the famous artist Verrocchio. As a result of this young Leonardo was enrolled as a student of Verrocchio's in Florence sometime between 1464 and 1470 (12 and 18 years of age). Leonardo stayed with Verrocchio after being admitted to the painters' guild in 1472. It was through Verrocchio that Leonardo developed his multitudinous interests. In fact he later surpassed his teacher who responded not with jealousy, but rather by collaborating and further advancing the gifts of his student. It may have been through Verrocchio that Leonardo got his start in the study of anatomy. However, the study of anatomy by painters of that time was designed primarily to teach them the form of the nude human figure for purposes of painting. In this early period Leonardo was probably no more than a spectator at public anatomies, and the earliest anatomical drawings available (1487) show no real knowledge of anatomy.

In 1483 da Vinci moved to Milan where he worked under the patronship of Lodovico Sforza. In his letter of introduction to Sforza Leonardo pictured himself as a man of great abilities in the fields of military engineering, mathematics, architecture, and sculpture. History has born out these immodest claims and has added to them such achievements as anatomy, comparative anatomy, physiology, civil engineering, and painting. During this "First Milanese Period" Leonardo became greatly absorbed with problems of geometry and mechanics but produced no tangible results in the fields of architecture or engineering. Most of his effort, however, was devoted to the construction of an equestrian statue of Francesco Sforza. In 1493 he completed a full scale model of this statue, but it was never cast in bronze. The final achievement of this period was the painting of the "Last Supper" begun in 1496.

Leonardo's studies in anatomy during this period were not extensive, although he did several detailed drawings on the anatomy of the horse. The earliest work on human anatomy, 1487, shows evidence of having been taken from the works of Avicenna and Mondinus, with only surface inspection of the living human. As early as 1489 there is evidence that Leonardo was considering more extensive study of anatomy when he makes reference to "The book entitled On the Human Figure" (3b). It was at this time that Leonardo developed his techique for cross-sectional representation of bones and the method of presenting anatomy from four aspects—"as though the viewer were able to walk completely around it and observe it from every aspect" (3c). The evidence suggests that Leonardo did not have access to a cadaver during his first Milanese Period, although he may have obtained a single human head and perhaps a thigh or leg.

After 1497 problems of war began to plague Sforza, and, as a result, Leonardo's salary went unpaid. In 1499 Sforza was forced to flee Milan, and Leonardo, at the age of 47, was forced to look for a new patron. He thus journeyed first to Venice, where he may have observed anatomies conducted by Alessandro Benedetti, and finally returned to Florence. It was here that Leonardo was able to take up the study of anatomy seriously, doing his dissections at the hospital of Santa Maria Nuova where he met his famed centenarian (*vide infra*). In spite of his easy access to anatomical material and his inquiring mind, however, Leonardo was still under the classical influence of Galenical authority as shown by his persistence in depicting man with a five-lobed liver (3d). He persisted in attempting to fit information obtained from animal dissection to the human form.

Among Leonardo's achievements during this "Florentine Period" was the technique of obtaining a mold of the ventricles of the brain by injecting them with wax. It was at this time also that he painted the famous "Mona Lisa" and constructed his flying machine. As usual Leonardo's efforts were directed in

many different directions with few major accomplishments in any.

As a result of family difficulties and the possibility of patronage, Leonardo left Florence in 1506 and returned once more to Milan to work for the official regency of the city. One accomplishment attributed to da Vinci at this time is the development of the canal system under construction in the Lombard plain. His work in anatomy also increased in both quality and quantity, spurred on somewhat by his association with Marcantonio della Torre, professor of the Theory of Medicine at Padua. According to a contemporary biographer, Vasari, Leonardo and della Torre planned to collaborate on a treatise on anatomy, the former doing the drawings with the latter supplying the text. The premature death of della Torre of the plague in 1511 ended the plans, and no evidence of the work has ever been found.

Further political upsets in 1512 forced Leonardo to leave Milan, this time permanently. He moved to Rome where he carried on studies in anatomy, distillation, physics, and optics until 1515. He then moved to the castle of Cloux near Amboise, France, at the invitation of Francis I, remaining there until his death in 1519. All of his notebooks were left to a young disciple, Francesco Melzi. The drawings then passed into obscurity until finally a large portion turned up at the Royal Library at Windsor. Just how they got there is not completely clear. The first effort to make them available to the public was in 1898. The book by O'Malley and Saunders (3) in 1952 is the first, and only, attempt to present the drawings with translations in systematic fashion.

"According to a horoscope cast by Jerome Cardan, the Milanese physician, mathematician, and epistolary friend of Vesalius, (Vesalius') birth occurred at a quarter to six on the morning of 31 December 1514, reckoned according to the Julian Calender. The place was Brussels, the chief city of Brabaut" (4a). Andreas Vesalius was the son of the apothecary to the Emperor Charles V of Austria and descended from a long line of men devoted to the cult of Aesculapius. This family heritage resulted in an extensive library of medical works which the young Andreas spent many hours reading. Very little is know of Vesalius' early life except that it was spent in Brussels, and that he was encouraged in his studies by his mother.

In 1528 Andreas Vesalius enrolled in the University of Louvain, where he received training in Latin with some Greek thrown in. During this time he spent many hours studying science, in particular anatomy. In his later writings he refers to the dissections which he performed at this time on animals of all sorts. In 1531, at the age of 17, Vesalius transfered to the Collegium Trilingue at Louvain, where he studied Latin, Greek, and Hebrew. His scientific leanings, however, prevented him from becoming a scholar in the sixteenth century meaning of the term.

Following this classical background, Vesalius went to Paris, in 1533, to study medicine. Although the University of Paris had a great name and wide-spread reputation, it was a very conservative institution. In the field of medicine this conservatism placed the school at considerable disadvantage in relation to the advances being made elsewhere, particularly in Italy. Although a knowledge of anatomy was required of all candidates for the bachelor's degree, there was no provision made for the teaching of anatomy by dissection. There were occasional "anatomies," in which the lecturer talked while an assistant dissected a body and the students merely observed. Vesalius probably attended no more than three or four of these anatomies during his stay in Paris. Most of the anatomy was learned from textbooks derived from the Medieval Arabic tradition and translations of classical Greek authors through Arabic and back into Latin—the language of scholars. A new contribution to the field of anatomy at this time was a Latin translation of Galen directly from the original Greek. Like other students of his time, Vesalius had no choice but to accept the Galenical anatomy. His greatness lies in his

refusal to accept this authority without question, but rather to seek confirmation and to note discrepancies by the observational method.

Vesalius left Paris without graduating and returned to Louvain in 1536. His departure was necessitated by the outbreak of war and the invasion of Provence by Charles V. In Louvain he continued his studies of anatomy, obtaining a skeleton by the discovery at the side of the road of a dried cadaver which he disarticulated and carried to his home piecemeal. Later, however, he was able to obtain bodies from the Burgomaster and conducted several anatomies.

In 1537, having completed his Baccalaureate, Vesalius journeyed to Basel where he had his thesis reprinted. He then set out for Italy and the University of Padua to continue his studies. The opportunities for study of anatomy and medicine at this time were greater in Italy than elsewhere in Europe. "On 5 December 1537 the faculty of the University of Padua, after examining Vesalius, granted him at a solemn convocation the degree of Doctor of Medicine 'cum ultima diminutione,' which represented 'with highest distinction,' and thus Vesalius was required to pay a fee of only seventeen and a half ducats, diminished in accordance with the excellence of the examination. On the following day after performing a dissection, he was nominated by the 'Illustrious Senate of Venice' as Professor of Surgery (at Padua), an appointment which at that time bore the responsibility of teaching anatomy as well" (4b). Vesalius was now 23 years old.

In his teaching of anatomy Vesalius broke with tradition by descending from his academic chair to dissect and demonstrate personally on the cadaver. To aid in his discussions he made up several large charts demonstrating the nerves, arteries, and veins. These were so popular that he had them printed, adding to his drawings three views of a skeleton drawn by Jan Stefan van Kalkar, a student in Titian's workshop in Venice. Judging by the many immediate plagiarisms, these plates, now known as the "Tabulae Anatomicae Sex," were an instantaneous success. This use of illustrations to teach anatomy was a completely new idea. Many of the physicians of the day were opposed to illustrations of any books on the grounds that this had not been done in classical times and would degrade scholarship.

At the end of his letter of dedication of the "Tabulae Sex," written to Dr. Narcissus Parthenopeus, physician to Charles V, Vesalius writes "If I shall find this work acceptable to you and to students, some day I hope to add something greater" (4c). This is the first hint of the major work which Vesalius published in 1543 under the title "De Humani Corporis Fabrica." The "Fabrica" has been called the greatest single contribution to the medical sciences. It was this work which removed anatomy from the chains of the dark ages and paved the way for further advances not only in anatomy, but also in all fields of medical science. The text and drawings were intimately interrelated by an extremely complex system of cross-references which wove them into an integrated whole. If the drawings are studied alone, without reference to the text, a very false picture of Vesalius' knowledge of anatomy is obtained, for he often corrected errors in the drawings by his comments in the text.

Following publication of the "Fabrica" and its companion piece, the "Epitome," Vesalius gave up his position at Padua and offered his services as physician to the Emperor Charles V. Although he gained much knowledge and experience as a military surgeon, his contributions to the advancement of medicine were negligible. Following the abdication of Charles V in 1553, Vesalius transferred his services to the new Emperor, Philip II of Spain. He continued in this capacity until his death in 1564 as a result of a shipwreck while he was on a pilgrimage to the Holy Land. That Vesalius was never satisfied with his life as physician to the Emperor and longed for a return to academic life was revealed in a letter written

in 1564 to Gabriel Fallopius in which he said, "I feel that the ornaments of our art originate in that arena from which as a young man I was diverted to the mechanical practice of medicine, to numerous wars, and to continuous travels" (4d).

SOURCES OF ANATOMIC KNOWLEDGE

As previously stated, Vesalius knew well the works of such men as Galen and the various Arab writers. However, he also was able to study the human body at first hand by means of dissection. His study was aided by the fact that public opposition to dissections was disappearing fast, and cadavers were becoming more readily available. The main obstacle to the study of anatomy was the lack of some method of preserving the corpse. The result, in the hot Italian climate, was that dissections had to be completed rapidly, and even so there was serious decomposition of parts of the body. Although there has been some disagreement as to Vesalius' authorship of the "Fabrica," there is no doubt that his knowledge of anatomy was extensive and taken from actual dissection.

With regard to Leonardo, on the other hand, there seems to be some difference of opinion as to exactly how much dissection he actually performed himself. In Leonardo's earlier years public dissection was still relatively uncommon. When the early Renaissance students would demand the truth about anatomical knowledge and verification of the facts, the Church would answer: "Go to your Galen; he has written truly and all you need to know" (5). In spite of this handicap, it is generally believed that da Vinci observed anatomies in his early years as a painter. The real disagreement comes in regard to whether or not Leonardo did dissections himself in his later years. Roth states: "We are now certain that Leonardo did not dissect himself, but his dissections, as was then customary, were made by surgeons" (6). McMurrich counters by quoting the Italian author Solmi as stating that if Leonardo did not do his own dissections it is hard to explain his exclusion from the hospital at Rome as "a heretic and cynical dissector of cadavers" (7). O'Malley and Saunders are a little more liberal when they state:

> "Despite various assertions which have been made regarding the numerous dissections—presumably human—which Leonardo performed, the only evidence of human dissection which can be drawn from the notebooks seems as follows: 1) a human head and neck dissected during the first Milanese Period (1481–1499); 2) dissection of the centenarian and Leonardo's statement of having dissected a child of two years, during the Florentine Period (1500–1507); 3) dissection of a human foetus around 7 months; 4) the dissection of the series in Fogli A which seems to have been that of an elderly man and perhaps the body of a younger individual; 5) perhaps a leg. Undoubtedly Leonardo was a spectator at other dissections" (3e).

Leonardo's own comments on his dissection of the centenarian would lead one to disbelieve the statement of Roth's that he did no dissection himself:

> "And this old man, a few hours before his death, told me that he had lived a hundred years, and that he did not feel any bodily ailment other than weakness, and thus while sitting upon a bed in the Hospital of Santa Maria Nuova at Florence, without any movement or sign of anything amiss, he passed away from this life.
>
> "And I made an autopsy in order to ascertain the cause of so peaceful a death, and found that it proceeded from weakness through failure of the blood and of the artery that feeds the heart and the other lower members, which I found to be very parched and shrunk and withered; and the result of this autopsy I wrote down very carefully and with great ease, for the body was devoid of either fat or moisture, and these form the chief hindrance to the knowledge of its parts.
>
> "The other autopsy was on a child of

two years, and here I found everything the contrary to what it was in the case of the old man" (8a).

Finally we have a statement by Keele that "later, in his last years at Amboise, Leonardo told the cardinal, Luis of Aragon's Secretary, that he had dissected 'more than 30 bodies,' and one may be sure he made drawings of them as well" (9). This is supported by Bailey who refers to a comment written by de Beatis of Leonardo when he was an old man at Amboise: "He has also told us that he has dissected more than thirty bodies of men and women of different ages" (5).

Regardless of the amount of dissection which Leonardo actually performed or observed, it is evident that he was well acquainted with the classical texts in anatomy of his day. He used these classical authors as guides in his observations, stating that "those who study only the ancients and not the works of Nature are step-sons and not sons of Nature, the mother of all good authors" (7). In his notes Leonardo frequently makes reference to such classical authors as Galen, Mondinus, Hippocrates, and Avicenna. Furthermore, Roth claims that "Leonardo's anatomy shows many relations to the literature, more abundant and more intimate relations than Leonardo's scanty citations of authors would indicate" (6). Finally, in his naming of structures Leonardo follows the pattern of Mondinus, taken from a Latin translation of Avicenna.

REASONS FOR DRAWINGS

For many years it has been believed that the reasons for doing the anatomic drawings were quite different with Leonardo and Vesalius. There is general agreement that Vesalius was motivated by a desire to find some means of teaching practical anatomy to the medical students of his day. The whole design and layout of the "Fabrica" suggests "an obvious desire to teach the subject and make it known to all and sundry, to get the details of anatomical structure inside of people's heads" (11). He was further motivated by his intense thirst for knowledge and desire for truth, a product of the Renaissance sweeping the continent at that time. Yet Vesalius had little use for the artists who crowded around his dissecting table eager for a glimpse of the workings of the human body. He writes in his China Root Letter:

> "As for those painters and sculptors who flocked around me at my dissections, I never allowed myself to get worked up about them to the point of feeling that I was less favored than these men, for all their superior airs" (10).

Many people have felt that Leonardo was prompted in his study of anatomy by the need for knowledge of the human form for his artistic endeavors. Streeter, in discussing the roles of Florentine painters in the history of anatomy, states:

> "To invest tense thought with sensible shape, to stimulate the moral will of the beholder, in fact, to tell a moving story convincingly and well in a representative form, at once religious and dramatic, required of the plastic artist that he unfailingly possess all that his forerunners had acquired in the knowledge of process and materials, and that he keep abreast of his time in subjects such as the chemistry of colors, the mathematics of composition, the geometry of perspective, the illusions of chiaroscuro, and above all, the science of human anatomy" (10).

A study of Leonardo's notebooks, however, suggests that he also was interested in teaching anatomy. His earlier efforts in learning anatomy were related to his painting, but his natural curiosity soon led him to study anatomy for its own sake. Keele (9) presents evidence to suggest that da Vinci became dissatisfied with the teaching of anatomy by public anatomies and thus proposed his treatise on anatomy, thinking of it as a means of teaching the subject to all men. Keele goes on to say "it is probably true that he did complete his project; at least he refers to 120 books about it" (9). Of this work we now possess 200 sheets of anatomical illustrations, "and those were entirely lost for nearly 300 years!" (9). It is this treatise on anatomy of da Vinci's which

Jackschath (2), in 1902, claimed was preserved for us in the "Fabrica" of Vesalius, thus accusing Vesalius of plagiarizing wholesale from the work of Leonardo.

In view of Vesalius' feelings toward painters, it is interesting to note that da Vinci once referred to the medical profession in a similar tone, saying "Try to preserve your health—and the best way to do this is to keep as far away from any physician as you can" (12).

THE DRAWINGS

Although it is now fairly well established that both Leonardo and Vesalius did actual dissections from which they made their drawings, each man has been accused of committing errors of greater or lesser magnitude. Since Vesalius' "Fabrica" has been available to the public for so much longer, it is natural that more criticism should be aimed at this work. Almost from the time the "Fabrica" was published other anatomists have been accusing Vesalius of errors and plagiarisms. John Kaye (1510–1573) wrote of Vesalius: "He renders Galen's text more corrupt than it was before, with no other view than that he might have somewhat to find fault with" (13). Another contemporary writer, Johannes Leon, wrote: "It is surprising that Vesalius, while he accuses Galen, the chief of physicians and anatomists, of so many blunders and errors, should yet himself be so justly liable to censure in the same respect" (13).

Most of the criticism of Vesalius' accuracy as an anatomist is based on two drawings, both of muscles. In one of these drawings Vesalius shows the Scalenus Anticus muscle of a dog, while in the other he shows extension of the Rectus Abdominis muscle up onto the chest as seen in the ape. The critics claim that these two drawings show that Vesalius was blindly following the mistakes of Galen without observing for himself. However, on examining the complete text of the "Fabrica" it will be seen that in each of these drawings the involved muscle is represented by an explanation in the text. Concerning the Scalenus Anticus muscle Vesalius writes:

> "Since in this place there is nothing else particularly that has appeared in man in this seventh diagram, and because I have leaned more toward the opinion of Galen when I made these drawings, you see here the muscle of a dog. . . " (14);

and of the extension of the Rectus Abdominis muscle:

> "Therefore if you scrape away the material in the intervening space, this is noted regarding the rectus abdominis muscle of an ape, that it is stretched out like a membrane" (14).

Thus it appears that Vesalius knew that he was representing the anatomy of animals and not man. Some authors have suggested that he did this deliberately to point out the mistakes which Galen made, possibly to prove that Galen never dissected humans. In this regard it is interesting to note that the Index of the "Fabrica" contains 214 references to Galen, most of them concerning some error in his work. Part of the difficulty with understanding the full meaning of the drawings and text of the "Fabrica" arises from the fact that "the Latin is so often very condensed with connecting words omitted, that one has to interpret as well as translate" (15). The interpretation is difficult for one not familiar with anatomy, while the translation is difficult for any but students of Latin.

When the drawings in the "Fabrica" are examined one is struck with the detail and life which was achieved in doing the woodcuts. The figures seem to be alive and active. "It is a special mark of the genius of Vesalius that he succeeded in portraying the muscles as if in the state of contraction required to produce the particular position given to the figure" (16). He also managed, by proper positioning, to include a great deal of material in each drawing, thus cutting down on the required number of drawings. For example, the skeleton shown leaning on a monument is in such a position that almost all the bones are shown, and most of these in at least two views, the most notable exceptions being the interior of the skull, the

posterior aspect of the sacrum and coccyx, and the upper thoracic vertebrae. This particular drawing also includes separate delineations of the hyoid bone and the ossicles of the ear, apparently to aid students in enumerating the number of bones. Vesalius himself had little interest in the prevalent controversy concerning the number of bones in the body, remarking, "if you count all the bones as seen in children, good God, what a great pile of bones you will heap up!" (4e).

Not all the drawings in the "Fabrica" are of such a high quality. The concensus is that most of the drawings were done by skilled artists and draughtsmen, probably in Titian's workshop in Venice, under Vesalius' direct supervision. There is some support to the idea that the drawings were even done by Titian himself. However, some drawings are of such inferior quality that it is suggested that they were either done by Vesalius himself or in a rather hurried manner by someone else. This is particularly true of the representation of the female genitalia (4f). Baker (17) disagrees with the prevailing view, claiming that Vesalius was an artist in his own right and could very well have done all the drawings himself. Baker further states that the drawings had to be done by someone intimately familiar with anatomy. These arguments, however, do not explain who did the carving of the woodcuts from the original drawings. Just where van Kalkar fits into the picture has not been settled. He is known to have been the artist for the preceding work, the "Tabulae Sex", but probably did not do many, if any, of the drawings for the "Fabrica" (16).

With regard to Leonardo's drawings, there is certainly no question but what he did them himself. Choulant (18) claims that the drawings are more accurate than those of Vesalius and are not approached in artistic beauty until the time of Soemmering and Scarpa (circa 1770). As with Vesalius, however, Leonardo is guilty of some errors of observation and in some instances of following earlier teaching blindly. This is particularly well shown in the description of a drawing of the portal circulation in which Leonardo ascribes five lobes to the human liver:

> "The vein which extends from the porta of the liver to the porta of the spleen has its roots in the 5 branchings which ramify in the 5 lobes of the liver" (3d).

The classical source of this error was Galen, and it showed up again in the Second Salernitan Anatomical Demonstration, written around 1100–1150, in which the author states:

> "Although the number of lobes (of the liver) varies in different animals, there are five in the pig, as I have recently shown you, and certainly the same number occur in man" (19a).

Classical anatomists felt that the internal anatomy of the pig was the same as that of man, although the external anatomy was different. In another instance there is a drawing of the human torso which is so inaccurate and clumsy as to suggest that it was done from memory rather than from a dissection, giving further support to the opinion that Leonardo was primarily an artist, not an anatomist.

One of the most noticeable differences between Leonardo's drawings and those of Vesalius is the age of the subjects. Most of Leonardo's figures are of old people, primarily the centenarian, while Vesalius tried to get young, healthy adults. Also the skeleton which Vesalius used was that of an 18 year old boy and thus shows epiphyseal lines, while few of Leonardo's bone drawings show the epiphyses. "Leonardo's representation of the skeletal system is one of the outstanding features of his work, but all the evidence seems to suggest that at no time did he ever possess an intact skeleton" (3e).

MORAL ASPECTS OF ANATOMY

An important aspect of the study of anatomy in the 15th and 16th centuries was the moral element. The writings of both Leonardo and Vesalius show that they were concerned with this problem and tried to justify their position

in dissecting the human body. As I have noted above, the church opposed any attempt to learn the truth about the inner works of the house of our soul. The most famous example of this attempt at justification in the writings of Vesalius is found in the drawing of the skeleton leaning on a monument. The inscription on the monument reads: "Man's spirit lives; all else death's hand shall claim" (16).

From Leonardo's works we have at least two passages concerned with the moral aspects of dissection. In "Anatomia, Fogli A, Folio 2 recto" is found the following statement:

> "And thou, O man, who learnest to know the marvels of nature through my work—if you believe it is a crime to dissect the human body, then stop to meditate, how much more criminal it is to take a man's life; and if this his outer form appears to you a wonderful structure, then remember that it is like nothing when compared to the soul living therein; for this soul, whatever it may be, belongs to God. Therefore, let it dwell in His work according to His will and pleasure and never permit your ire or malice to destroy such a life. For it is everlastingly true that whoever does not respect life is unworthy of possessing it" (12).

At another place in his writings Leonardo says:

> "O speculator on this machine of ours, let it not distress you that you give knowledge of it through anothers' death, but rejoice that our creator has placed the intellect on such a superb instrument" (8b).

INFLUENCE ON ANATOMY

The final point of comparison between these two men concerns their influence on the field of anatomy and the general public both at the time they lived and at the present. Since the works of Leonardo have only recently come to light, many authorities feel that he should be given no place in the development of the science of anatomy. They maintain that Vesalius was the true father of anatomy.

First, however, we must define "anatomy." According to the Second Salernitan Anatomical Demonstration:

> "Knowledge of all these things is gained in many ways; from anatomy we learn their position and difference of structure and we get a simple and clear demonstration of their form. The word 'anatomy' is derived from 'ana,' or equal, and 'tomos,' a division; hence an anatomy is an orderly dissection" (19b).

If we use this definition of anatomy, both Leonardo and Vesalius were certainly great men in the field. Both conducted orderly dissections and rendered clear and simple demonstrations of the forms observed in their drawings.

We come then to the question of who actually founded the science of anatomy. Certainly Leonardo did his work before Vesalius was more than an idea in his father's mind. Yet Garrison supports Vesalius when he writes:

> "What do we mean by the 'Founder' of a science? It is not he who has made that science viable and accessible and practicable to all mankind, respected by all mankind? . . .
>
> "The illustrations in the 'Fabrica' are not, as with Leonardo's 'Quaderni,' the communings of a great creative and scientific artist with himself, but suggest an obvious desire to teach the subject and make it known to all and sundry, to get the details of anatomical structure inside of people's heads" (11).

Garrison further points out that, in his attempt to establish anatomy, Vesalius incurred the ridicule of his contemporaries and perhaps even risked his life. It is certain that Vesalius had a profound effect on the thinking of his day and, with the publication of the "Fabrica," put the study of anatomy on a firm basis.

However, no man really establishes something such as the science of anatomy completely *de novo*. There has always been previous work which permits someone with proper training, incentive, and insight to make the necessary advance. Thus it is possible that, although Leonardo's work was not published in his day, it still played an influential part in the

progress of anatomy of the Middle Ages which culminated in Vesalius' "Fabrica." Baer suggests that Leonardo's share in the development of anatomy has been grossly underestimated, stating that there were other means besides the printed word for the diffusion of ideas. He then quotes Klebs as saying "mind has always bespoken mind even before the invention of the printing press" (12).

When the works of these two men are viewed today, apart from their influence on the progress of anatomy, both are recognized as great thinkers and observers. Baker says of Vesalius that he can be said to have discovered the correct gross anatomy of the entire body, "as there is no region that he did not illuminate by his observations" (17). Vesalius was one of the first physicians to break with Galenical authority and make his own observations. His published works are recognized as scientifically accurate and artistically beautiful. When it is realized that the printing was done from woodcuts, the clarity of the type and drawings is amazing. Few works of today surpass the precision and beauty of the original edition of of the "Fabrica."

With regard to Leonardo, however, some people hesitate to rank him among the greatest men of his day, since in the field of anatomy, as in all other fields in which he worked, he did not complete anything. Thus he has left us, not a finished treatise on anatomy, but rather a collection of sketches and excuses for his failure to complete the proposed work. Washburn (13), however, feels that since Leonardo studied anatomy by actual dissection and did excellent drawings of the materials, he should be ranked among the top anatomists of his day. Bailey further comments that "he is to be judged by his insight and the breadth of his conceptions rather than by his finished products" (5).

Thus we have considered here two men, both of whom refused to accept classical authority, but rather insisted upon learning by observation. One had a profound influence upon the thinking of his day, while the works of the other remained lost to the world for over 300 years. It has been the purpose of this paper to compare the men as fairly as possible. To the reader is left the job of making his own value judgments.

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Memoir of James Reid Martin, (1887–1956)*

By THEODORE R. FETTER, M.D.

DOCTOR JAMES REID MARTIN, a son of a Philadelphia physician, Doctor Joseph Martin, a graduate of Jefferson Medical College of the Class of 1878, was born in Philadelphia on February 8, 1887, and died on December 26, 1956. He had a rather prolonged last illness but during this incapacity he maintained almost daily contact with his office and work as Associate Dean of his *Alma Mater*.

James Reid Martin was graduated from Jefferson Medical College in the year 1910. He was awarded the Honorary Degree of Doctor of Science at the commencement exercises in June 1951. Almost continuously from the time of graduation from Jefferson Medical College, until his death, he was connected with the teaching and Administrative Staff of his *Alma Mater*. He was also an active member of the Philadelphia Central High School Alumni Association.

Following his graduation from medical college, Doctor Martin served as an intern and later as Chief Resident Physician at the Jefferson Medical College Hospital. Thereafter, he became associated with the Department of Orthopedic Surgery. Because of his accomplishment as a teacher, surgeon and investigator, he advanced to Assistant Professor of Orthopedic Surgery in 1930. He was appointed James Edwards Professor of Orthopedic Surgery and Head of the Department in 1939 and held this position until his retirement in 1950 when he became Professor of Orthopedic Surgery, Emeritus. He was appointed Associate Dean of the College in March, 1950 and was serving in this capacity at the time of his death. He is survived by his widow, Florence Hale Martin.

Doctor Martin's accomplishments and associations were many and varied, not only in the field of his specialty but also in civic, religious and humanitarian groups. He served in World War I, from 1917–1919, as medical officer in the 109th Infantry of the 28th Division, serving overseas. After the Armistice he was on the orthopedic staffs of various Base Hospitals of the American Expeditionary Forces. Following his return to civilian practice he became associated with numerous hospitals in Pennsylvania and New Jersey as consultant in Orthopedic Surgery. He was also affiliated with the State Hospital for Crippled Children at Elizabethtown, and became Director of the Social Security Program for Crippled Children in the State of Pennsylvania. He served for many years as Chief in Orthopedic Surgery at the Philadelphia General Hospital and contributed tremendously to the development of the Department of Orthopedics at that institution. He made noteworthy contributions in orthopedic surgery and was particularly interested in establishing good orthopedic practice in smaller community hospitals.

Doctor Martin had an extraordinary character. He was not only a renowned physician, surgeon and teacher, but a benevolent humanitarian. His kindly works and deeds were only known to a small group of friends. He was an Elder of his Church and teacher in its Sunday School for many years. He was a Christian in the highest sense of the word. His loyalty to his college, his service to his Church, his integrity and faithfulness made him an admired and respected, devoted friend. During the latter months of his life, several of us had the privilege to participate in his thinking and philosophy of life and service to his fellowman. His sincere belief in the Almighty made his last year comfortable—in every sense of the word.

A very close friend and associate, Dr. Erwin D. Funk writes: "Dr. Martin needs no eulogy from those who knew him well, for 'To live in the hearts of those we love is not to die,' and 'Jim,' as we fondly called him, will live on."

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

Memoir of Edward J. G. Beardsley (1879–1956)*

By FRANCIS F. BORZELL, M.D.

TO WRITE of the passing of some men may present a difficult task. In an effort to be kindly, absolute frankness in some instances may not be desirable. On the other hand, the death of a nobleman may tempt one to be overeffusive. The difficulty in this instance is that no words or phrases can do full justice to the life of Edward John Gillespie Beardsley. His passing marks the end of a lifetime of devotion to the highest ideals of the medical profession.

John Beardsley was born in a little white house by a lovely brook in the hilly and stoney little town of Roxbury, Connecticut, on May 31, 1879. His father was Lewis Bielkeley Beardsley who descended from a long line of distinguished New England families. He was born in 1857 and died in his 27th year, of typhoid fever. He left a young wife and two children, John, aged 7, and Grace, aged 5. Dr. Beardsley's mother was Mary Agnes Gillespie, of Scotch parentage—a woman of most extraordinary character and vision, which was lastingly reflected in the life and character of her son John. The family was poor in worldly goods but rich in a heritage of a sturdy and noble ancestry. Her passing during John's senior year at Jefferson Medical College was a deep and enduring sorrow to him.

Dr. Beardsley's ancestry dates directly back to 1635 when William and Mary Harvey Beardsley landed in Massachusetts from the ship "Planter." William Beardsley settled in Stratford, Connecticut, and later established the Congregational Church there. His descendants took an active part in forming our New England history. One Robert Beardsley married Hannah Chauncey, a daughter of the second President of Harvard College. John himself was a direct descendant of Oliver Wolcott, one of the signers of the Constitution of the United States.

John worked his way through school and College. He came to Philadelphia and after two years at the Philadelphia College of Pharmacy, matriculated at Jefferson Medical College where he was graduated in 1902. He served his internship at the Philadelphia General Hospital and the Municipal Hospital for Contagious Diseases. Following a year of study in London he became a licentiate of the Royal College of Physicians. Returning home, he entered the practice of medicine at Philadelphia in 1906. Two years later he was appointed Demonstrator of Clinical Medicine at Jefferson. He gradually advanced from one appointment to another until he was made Clinical Professor of Medicine, in 1927, a post which he held until 1941 when he resigned to accept the Chair of Medicine at Woman's Medical College of Pennsylvania. He was also Physician in Chief to the Municipal Court, which position he held until the time of his death.

Dr. Beardsley served with distinction in the First World War. He retired as Lieutenant Colonel after serving under General W. Crawford Gorgas at Washington and Fort Oglethorpe, and with the 89th Division in France.

He was elected a Fellow of the College of Physicians of Philadelphia in January 1908. He served as Clerk and Chairman of the Section on General Medicine, and the Section on Medical History. He was Chairman of the Committee on Scientific Business and served on various other Committees. He served as a Councillor from 1938 to 1941 inclusive. From 1953 to 1956 he served, by appointment of Dr. Kern, on the Community Nursing Bureau.

For many years and until his death, he was a member of the Board of Directors of the Aid Association of the Philadelphia

* Read before the College of Physicians of Philadelphia, 6 November 1957. Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

County Medical Society, exhibiting all the unselfish devotion that so endeared him to everyone.

Those of us who were privileged to know him as a teacher, a consultant and a man had our lives enriched and our standards elevated by his selfless exemplification of true idealism softened by a tender consideration for his fellow man. His students could not help but be strongly influenced by contact with Dr. Beardsley, the physician, humanitarian and counselor. Throughout his life he credited his mother with having inculcated the noble tenets that obviously governed him.

While always the champion of his profession and a dauntless defender of his colleagues, he unhesitatingly challenged any semblance of deviation from ethical standards. This facet of his character is illustrated in a comment he made on his experience as a member of the Board of Censors of the Philadelphia County Medical Society. He said of this: "Modern medical practitioners are all too often making a not-legitimate business out of what was intended to be a helpful profession."

In 1944 Dr. Beardsley underwent major surgery which almost cost him his life, and from that time on his health continued to fail. Dr. Beardsley's widow, in a communication to the writer, paid personal tribute to the services of Drs. David Kramer and David Cooper during the last few years of his life. The end came suddenly when Dr. Beardsley was struck and killed by an automobile on December 27, 1956.

Edward John Gillespie Beardsley was truly a Nobleman whose life has greatly enriched the history of medicine in Philadelphia.

Memoir of George Edward Pfahler (1874–1957)*

By JACOB H. VASTINE, 2nd, M.D.

DOCTOR GEORGE EDWARD PFAHLER was born in 1874 in Numidia, Pennsylvania, son of William and Sara (Stine) Pfahler.

He was educated at a local ungraded country school, and began his career as a school teacher in 1892; graduated from the Bloomsburg State Normal School, now Teachers College, in 1894. He graduated from the Medico-Chirurgical College of Philadelphia in 1898, and served as Resident Physician during 15 months, then as Assistant Chief Resident Physician in the Philadelphia General Hospital for three years. At that time he became interested in Radiology and was director of the Department of Radiology at the Philadelphia General Hospital from 1899 to 1903, and Director of the Department of Radiology at the Medico-Chirurgical Hospital from 1902–1918. He was made Clinical Professor of Radiology at the Medico-Chirurgical College in 1909, and served as full Professor of Radiology from 1911–1916. At the end of this period, the Medico-Chirurgical College amalgamated with the University of Pennsylvania. In 1916 he was appointed Professor of Radiology and Vice Dean of the Department of Radiology in the Graduate School of Medicine of the University of Pennsylvania, a position which he filled for thirty years. He served as Director of the Radiological Department of the Graduate Hospital in Philadelphia from 1916–1932, and as Director of the Radiological Department at the Misericordia Hospital from 1916–1943.

His interest in pedagogy began as a teacher in a little red school house. This followed through his life and at the time of his death he was on the Board of Directors of Ursinus College at Collegeville, Pennsylvania.

Doctor Pfahler was primarily a Physician, interested in the humanities of life. He possessed no social aspirations, although he could trace his ancestry back to German Royalty. He had a singleness of purpose and solid devotion to his profession and specialty. He gave his life literally to help his fellow men, dying of leukemia on January 29, 1957, probably as the result of many years exposure to irradiation.

The success of this dedication to his patients is documented in the 334 contributions to the Medical Literature which he made over a long and fruitful life.

He gave unstintingly of his time and energy to his specialty, of which he was one of the pioneers. This is attested to by the fact that he served in the following capacities: President of the American Roentgen Ray Society from 1909–1910; President of the American Electro-Therapeutic Association from 1912–1913; President of the American Radium Society from 1921–1922; First President of the American College of Radiology from 1922–1923; President of the Medical Club of Philadelphia in 1955; President of the Aid Association of the Philadelphia County Medical Society from 1952 to 1957, and President of the Dermatological Society of Philadelphia from 1956–1957.

He served as Chairman of the Committee on Cancer Control of the Philadelphia County Medical Society, Philadelphia, for nineteen years; Chairman of the Executive Committee of the American Cancer Society, Philadelphia Division, for seven years, and, at the time of his death, was a Member of the Board of Directors.

Doctor Pfahler served on the Executive Committee of the First and Second International Congresses of Radiology in 1925 and

* Read before the College of Physicians of Philadelphia, 6 November 1957. Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

1928; was Honorary Vice President of the Fifth International Congress of Radiology, held in Chicago in 1937. He was named Honorary Vice President of the Sixth International Congress of Radiology held in London in July, 1950; Vice President of the Seventh International Congress of Radiology held in Copenhagen in 1953, and was named Vice President of the Eighth International Congress of Radiology held in Mexico City in July, 1956.

His tireless efforts were recognized both here and abroad by Honorary Memberships in the following Societies: Honorary Member of the Radiological Society of North America; Honorary Member of the National Gastroenterological Society (1955); Honorary Member of the Radiological Societies of France and of the German Roentgen Society; The Radiological Society of Russia; the Radiological Society of Scandinavia; The Radiological Society of Austria; The Radiological Society of Cuba; The Radiological and Physiotherapy Society of Mexico; Sociedad Radiologica Panamena; Sociedad Peruana de Radiologia; Honorary Member of the Radiological Section of the Royal Academy of Medicine in London; Honorary Fellowship of the Faculty of Radiologists of London in 1950; Honorary President of the Alumni Association of the Graduate School of Medicine, University of Pennsylvania, in 1950.

In addition he was a member of the American Medical Association; Philadelphia County Medical Society; College of Physicians of Philadelphia; the American College of Physicians and the National Gastroenterological Society.

The following are some of the Medals and Awards which he has received: The Strittmatter Gold Medal of the Philadelphia County Medical Society in 1930; the Gold Medal of the American Radium Society in 1935; Gold Medal of the America Roentgen Ray Society in 1937; Gold Medal of the Radiological Society of North America in 1952; First Medal of the Centre Antoine Béclére of Paris in 1952. This medal was presented to Doctor Pfahler personally by Mlle. Antoinette Béclére at the Inter-American Congress of Radiology in Washington on April 28, 1955.

Award of Merit from the American Cancer Society in 1945; Award of Merit from the Medico-Chirurgical College Alumni Association in 1948; Distinguished Service Award and Life Membership from the State Teachers College Alumni Association in 1950; Award of Merit from the American Medical Association Foundation in 1951, and the Award of Merit from the American Society of X-ray Technicians in 1953.

The Science Building at Ursinus College was dedicated *Pfahler Hall of Science* in recognition of his achievements in his chosen field.

One of the greatest compliments paid Dr. Pfahler was the dedication of the "Lehrbuch der Roentgen Diagnostik", written by Prof. Dr. H. R. Schinz, W. Baensch and E. Friedl, to the five pioneers of Roentgenology, naming: Henrich Albers-Schönberg of Germany, Antoine Béclére of France, Gosta Forssell of Sweden, Guido Holzknecht of Austria, George E. Pfahler of America. This work covers 3792 pages of "roentgen diagnosis literature."

Doctor Pfahler also felt especially complimented when Manuel and Francisco Arce of Madrid, Spain, dedicated their book, "Radiodiagnostico En La Infancia," (Madrid Ediciones Boro, Tudescos, 41, 1933.) to the following world leaders in Radiology: A. Béclére and J. Belot of France; A. Busi, V. Maragliano and F. Perussia of Italy; A. Köhler and W. H. Meyer of Germany; George E. Pfahler of America; H. R. Schinz of Switzerland.

He was a man who spurned all frivolities or other activities outside his *curriculum vitae.* I cannot close with such a brief dismissal of his personal life. He and and Mrs. Pfahler were members and supporters of St. Asaph's Episcopal Church, Bala. His religious feeling and interest in the humanities is evidenced by the bequeathal of almost his entire estate ultimately to return to those who made his

life so complete—the physicians of Philadelphia, through the County Medical Society, to establish scholarships for deserving students.

In 1908 Doctor Pfahler married Miss Frances Simpson, daughter of Judge and Mrs. Alexander Simpson. She died in 1910. In 1918 he married Miss Muriel Bennett, a close friend of the Simpson family. They enjoyed a companionship for almost forty years. Mrs. Pfahler's chief rival was Prince—a dog. In closing, we note that it is always a good sign when a man likes a dog.

TRANSACTIONS & STUDIES
of the
College of Physicians of Philadelphia

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Number 4
(April 1958)

President's Address

By LEWIS C. SCHEFFEY, M.D., SC.D. (HON.)

THE purpose of the annual address of the President is to inform the Fellowship of what has transpired during the year past, to acquaint them with the progress of the institution, and to inform them of the problems that await consideration. I have done so twice before. This time, in addition to the annual report on the state of the College, I speak as your retiring President, soon to present my successor to you.

Much of the information that would ordinarily go into an address of this sort has been presented to the Fellowship rather promptly in the series of "Newsletters" you have received throughout 1957. Hence detailed repetition of many items already published is time consuming to relate and expensive to reprint.

As I look backward, the years of this administration may be indexed specifically with respect to accomplishment in this order:

1. 1955—the successful culmination of the fund-raising campaign to construct the needed book-stack addition and to rehabilitate the present building.

2. 1956—the actual completion of the program and payment in full for same.

3. 1957—creation of a sound and permanent fiscal policy for the College, including acquisition of neighboring property as part of our investment program, and finally the stabilization of the General Endowment Fund and the College Extension Fund, each of which serves an independent purpose for the continuing benefit of the College.

None of this could have been accomplished without the substantial help of many Fellows of the College, their friends, and the liberal support of the Donner, Pew and Kresge Foundations. To these acknowledgements I add the continued confidence of the Fellows of the College in the policies of our Administration, as attested by the large and positive votes in favor of them.

STATUS OF THE FELLOWSHIP

Sixteen Resident and three Non-Resident Fellows died during 1957—19 in all. Let us stand together in silence as we give thought to the memory of those departed from us:

Resident

Everett P. Barnard
Ralph S. Bromer
Williams B. Cadwalader
Lawrence Curtis
Frank C. Knowles
Simon S. Leopold
John P. Lownes
Paul M. Mecray
George E. Pfahler
Harry E. Rothrock
John B. Roxby
Winifred B. Stewart
George W. Wagoner

Benjamin P. Weiss
Nathaniel S. Yawger
Frederick O. Zillesen

Non-Resident

Anthony R. Camero
William Penn Vail
De Forrest P. Willard

As of December 31, 1957, the entire Fellowship of the College numbered 1130, distributed in the following categories: 988 Resident, 132 Non-Resident, 1 Associate, 4 American Honorary, 3 Foreign Honorary, 2 Honorary Associates. This represents a net gain of 20, the same number as one year ago.

Although there has been a small gain in overall membership during the past three years, the new Resident Fellows have just about equalled the number who died during 1956 and 1957. The ratio between Resident and Non-Resident Fellows has not altered either during these years, but the Non-Residents have increased progressively from 106 to 122, and finally to 132 in 1957. It is important that greater efforts be made to bring more of our colleagues into the College. The Special Committee for Promoting Proposals for Membership is representative of all of our academic and hospital areas, and its efforts may be reflected more clearly during the months ahead. Furthermore, it seems to me that each Fellow should assume personal responsibility in seeing to it that younger physicians of repute and promise among his acquaintance should be made aware of the honor and advantage of becoming Fellows of the College, and proposals prepared for them. It is obvious that a suitable increase in the Fellowship is essential if the growth and vitality of the College is to be maintained.

ADMINISTRATIVE STAFF OF THE COLLEGE

With respect to the Library, the Medical Literature Service came of age this year with the establishment of the Medical Documentation Service that is attracting more and more attention locally and abroad. An important meeting at the College on November 27 last, brought together representatives from the research laboratories of renowned pharmaceutical firms, scientists, editors, industrialists, publishers, librarians and educators who met with members of the Library Committee, Staff and Officers of the College to discuss ways of implementing the service and supporting it more substantially. The outcome was on the positive side and encouraging to Elliott Morse, our devoted Librarian, and especially so to Miss Walsh, the Assistant Librarian who directs this Service, and of which Mrs. Stevens is the efficient Executive Secretary. There were few changes in Library personnel during the year. Miss Colabrese left to become librarian at the Eastern Psychiatric Hospital; Mrs. Pellicano (*née* Ceci) secured a position elsewhere, and Miss Ella Wallace was advanced to Reading Room Assistant. The Misses Hodge, Zeldis, Minton, and Mrs. Miragliotta continue their efficient service in the Library.

W. B. McDaniel, 2d, Ph.D., who dislikes being called "Doctor," continues to grace the Packard-Krumbhaar Alcove and its activities as only he can. The "Fugitive Leaves from the Library" delight us continually and are eagerly awaited in the monthly mailings. His erudite associate in historical adventures, Dr. Fred B. Rogers, becomes more and more meticulous in his editorship of the "Transactions and Studies." The published annual report of the Library is eagerly awaited.

Miss Olga E. Lang, Clerk of the College, faithfully administers the affairs of the office in her own inimitable way, and the thanks of all of us go to her. Mrs. Terry Gredone, appointed during the past year, is a most capable assistant in this area.

The Superintendent of the College, Mr. George S. Allen, directs his staff wisely and well, accepting responsibility with energy and competence. The acquisition of the adjacent garage building as part of the College's investment program has added considerably to Mr. Allen's duties, to which he has measured up without hesitation.

The eighteen years of service to the College

by Mrs. Ella N. Wade, Curator of the Mütter Museum and Custodian of the College Collections, were fittingly observed on December 11th, and this happy occasion was described in the "Newsletter" of that month. Congratulations again!

OFFICERS COMMITTEES AND SECTIONS

On behalf of the entire Fellowship, I commend and thank the officers and members of Council who have given of their time, energy and wisdom to govern and promote the interests of the College. Thomas E. Machella has mastered his duties as a newly-elected Secretary most effectively and we congratulate our Ex-Presidential Councillor, O. H. Perry Pepper on his emergence as "author of the year." John E. Deitrick's resignation as an elective Councillor because of leaving Philadelphia was deeply regretted by his colleagues. J. Parsons Schaeffer, distinguished anatomist, educator and a past President of the College, will be missed in his position as Censor from which he voluntarily retired at the end of the year past.

The chairmen and members of the Standing Committees have attended to their duties and assignments with precision and devotion. Joseph Stokes, Jr., and the Publication Committee were actually shame-faced because of an unforeseen deficit due to astronomic rise in printing costs. The Library Committee, under the leadership of our beloved Burton Chance, a Fellow of the College since 1900, has profited by his wisdom and devotion as he approaches his 90th birthday. In his capacity as Librarian, Elliott H. Morse has been conscientious and able in aiding the Committee. The duties of the Hall Committee have been amplified by the expansion of the College property, the acquired garage building and responsibilities of maintenance. Joseph Vander Veer and his associates have given unstintingly of their time in serving the property interests of the College and aiding Mr. Allen in his responsible position. The Finance Committee has also done outstanding service to the College. The Chairman, Theodore R. Fetter, has enjoyed the counsel and wide experience of the recent Past Presidents, Grier Miller and Richard Kern, and that of the Treasurer, Jacob Vastine 2nd, his colleagues on the Committee. The Committees on Scientific Business, and Public Health, Preventive Medicine and Public Relations have had unusually fine leadership under David Cooper and Pascal Lucchesi respectively, to which the members have responded in cooperative fashion. Theodore F. Bach has been vital and energetic in his Chairmanship of the Mütter Museum and College Collections Committee. Harold G. Scheie and his Entertainment Committee still rest on the laurels achieved at the "open house" reception of 1956!

I remarked earlier concerning the problems of one of the Special Committees—that of promoting proposals for membership in the College. The other Special Committee—to act in liaison with a similar Committee of the Philadelphia County Medical Society to discuss closer relations between the two organizations—has held several meetings, but no conclusions have been reached as yet. I trust that the mutual endeavor of these Committees will be continued.

The decisions of the various Prize Committees and Trustees were evidently popular, for large audiences attended the lectures during 1957, and it is hoped that this will be equally true of those continuing into this year.

The programs of the various Sections held during the past year were excellent in scope and well-received, as will be noted later by the published accounts in the "Transactions and Studies." The new officers chosen by the Sections for 1958 are subject to appointment by the incoming President of the College.

Increasing problems of a legal nature arising in certain fields of activity of the College have required rather frequent recourse to Eric A. McCouch, Honorary Legal Counsel, and the gratitude of the Fellows and the Administration is extended to him for his discerning judgment and timely advice so graciously given and often without even modest compensation.

Relations with the Council for International Visitors remain cordial. Our Fellow, George M. Piersol, is Chairman of the Committee on Medical Visitors, and as the College of Physicians is the official source of contact in this particular field of activity, your President has cooperated effectively in this respect with Dr. Piersol and his associates. I strongly recommend that this policy be continued.

FINANCES

The year past is notable for the College because of the enabling legislation, effective as of 4–3–57, that made possible the consolidation of certain non-restricted trust funds and existent funds from other sources to establish: I. The General Endowment Fund, and also the creation of a needed auxiliary: II. The College Extension Fund.

GENERAL ENDOWMENT FUND

As of November 10, 1956, the book value of the various non-restricted trust funds transferred to the General Endowment Fund amounted to $328,065.83. Chapter XIV of the By-laws indicates the other sources that nourish this fund and enable it to grow. The receipts from the nine sources spelled out in the amendment, and received between 11/10/56 and 11/10/57, amounted to $19,463.01, thus increasing the book value of the General Endowment Fund to $347,528.84. Detailed figures from these sources appear in the accompanying Treasurer's Report, as published in the issue of the "Transactions and Studies" which accompanies this address. These unrestricted funds operate as part of a discretionary common trust fund, the income of which is currently paid to the operating account of the College for the appropriations that Council recommends for the yearly College budget. I acknowledge with heartfelt thanks a bequest from the John H. Gibbon Estate of $5,000, from the George E. Pfahler Estate of $1,000, and from the Kate Balentine Estate of $200, in memory of Percy L. Balentine.

COLLEGE EXTENSION FUND

This fund was created to anticipate future needs of the College along capital lines—as for major repairs, etc., the amount of which exceed in amount 25 per cent of the gross annual budget for that current year. It is dependent upon voluntary gifts and bequests from Fellows and friends of the College who have an awareness of the need for cushioning unusual and/or unexpected expenses that cannot be met out of current operating income, without borrowing. Income from this fund is added to principal, and Council may direct an annual appeal to the Fellowship for contributions to this Fund, which as of 11/10/57 amounted to $1,212.48.

Both of these funds are under the supervision of the Committee on Finance, under the rules and direction of Council, in the same manner as are other financial affairs of the College. The integrity of these funds is guaranteed by the authority of the By-laws; their structure cannot be altered by mere acts of Council. Thus the permanence of the Endowment Fund of the College and its future growth has been assured by these controls, incorporated on April 3, 1957 in the By-laws of the College by Fellowship vote.

THE RESTRICTED ENDOWMENTS

A further source of income, the receipts of which may only be used for purposes designated by the donors, are the restricted Endowment funds of the College. As of 11/10/56, their book value amounted to $549,458.96. The income from 11/10/56 to 11/10/57 amounted to $22,856.30, being utilized as specified. I announce especially, and with gratitude, the bequests of $5,000 from the estate of Margaret Farley deceased, and of $14,000 from the Harriet Sartain estate, both of which are restricted for the general needs of the Library. We also thank "The Friends of the George E. Pfahler Library Fund" who contributed $142.40.

OTHER SOURCES OF CONTRIBUTIONS

Other receipts from monies received from building fund pledges and voluntary contribu-

tions from Fellows and friends of Fellows to the Building and Development Fund amounted to $3,935.51. Life membership funds totaled $995.40, and the Pension Reserve Fund amounted to $469.26. The Mary Scott Newbold Lecture Fund yielded $1,023.84.

In summary, therefore, the total book value of the accrued funds that have been mentioned amounts to $921,056.58. All sources of revenue participate on a unit basis in the Discretionary Common Trust Fund, and as tabulated in the concomitant Treasurer's report.

BUDGET

In presenting the Annual Budget for the fiscal year of 1957–58, I commend those responsible for its preparation in these days of inflation coupled with rising costs of maintenance that parallel an enlarged plant, increased facilities and a newly acquired real estate investment. With all these factors in mind the Chairmen and members of the various Committees have tempered justifiable increases with generous restraint. Even so our anticipated income and anticipated expense are in balance, but at a gross overall increase in the budget of approximately $36,000. So all can realize why the annual contribution of the Fellows had to be raised from $50 to $60.

Anticipated Operating Income, 1957–58

Income, current operating account	$85,765.24
Income, publication Committee	1,189.98
Income, Committee on College Collections (Abbe Fund)	120.00
Income, Operation of Library	78,708.48
Total anticipated operating income	165,783.61
Total anticipated operating expense	165,331.56
Anticipated balance	$420.05

Appropriations, 1957–58

Secretary	$6,375.84
Treasurer	8,199.85
Publication Committee	5,315.60
Committee on College Collections	3,255.00
Hall Committee	29,031.88
Library Committee	110,630.25
Pension Reserve Fund	2,523.14
Total anticipated Operating expense	$165,331.56

As you probably know, there is a Maintenance and Reserve Fund apart from monies in the General Endowment Fund and restricted funds already discussed. This fund was set up in 1949 with $3500, accrued income from the Nurses' Directory that was discontinued in that year. Thereafter Council transferred surplus funds from the current operating account from time to time and in November 1956, with accrued interest, the total amount available for emergencies was approximately $23,000. The deficit in the budget that year amounted to $5843.53, and in 1957 it was $4,352.07. These deficits, necessitated by rapidly rising costs of maintenance in all quarters and coincident with the building and rehabilitation program, were met by payments from the Maintenance and Reserve Fund which has thus been reduced to $11,104.74. The Finance Committee, Council and the Administration feel in honor bound to restore this "borrowed" sum of $10,195.60 to the Fund as soon as it can possibly be done. Without incurring these deficits the services of the College to the Fellowship could not have been adequately rendered, or the loyal personnel been fairly treated, and I need not apologize for this. That is why I had hoped that my request for voluntary contributions to the Endowment and Extension Funds appearing in the November "Newsletter" would have met with a wider response before the time for 1957 income tax deductions expired with the New Year. It is still not too late! I hope that during the current year more and more of the Fellows will utilize the chances available for increasing the General Endowment and College Extension Funds as set up in the By-laws. All of us have loyal friends and patients who would gladly contribute to the College as a token of their appreciation, if it were only suggested to them. The "Book of Remembrance" offers an opportunity to memorialize those who leave us, far better than the flowers that wither "ere night falls." Finally, how many of us have thought of providing testamentary bequests for the College? I know full well that some have, and I urge all

the Fellows to give earnest thought to this suggestion.

In completing my three-year term of office as President of this venerable institution I can say without reservation that I have never enjoyed a finer experience in service to my colleagues than that afforded by my association with the College of Physicians of Philadelphia. I thank my associates for their loyal support and tolerance; truly "my cup runneth over."

It is with pleasure and satisfaction that I present to the Fellowship your new President and our staunch friend, the distinguished Provost and Professor of Surgery at the University of Pennsylvania, Doctor Jonathan E. Rhoads, to whom I happily present the Pfahler gavel.

Inaugural Remarks[1]

By JONATHAN E. RHOADS, MD., D. SC. (MED.)

DR. SCHEFFEY, Fellows of the College:

A POSITION such as the Presidency of the College of Physicians of Philadelphia is an honor which must be evaluated in terms of one's predecessors in office, in terms of the support of one's colleagues, and in terms of the opportunity it affords to further the accomplishment of worthwhile goals.

In terms of predecessors, there is no office restricted to physicians in this area which, in my opinion, has been filled by so many persons who have been my professional heroes and the heroes of many of us. The names of the founding group are well known to most of us, and later there were Dr. S. Weir Mitchell, Dr. William W. Keen, Dr. Francis R. Packard, Dr. Edward B. Krumbhaar, Dr. O. H. Perry Pepper, Dr. J. Parsons Schaeffer, and in the past three terms, Dr. T. Grier Miller, Dr. Richard A. Kern and Dr. Lewis C. Scheffey. While I cannot hope to bring to the College the prestige which these men and others have lent to this office, I do hope that by taking advantage of the opportunity which the office provides to help in accomplishing some of the common objectives which we share for the College, I can make some further contribution to this, the oldest of the medical organizations of the academy type in America.

Someone surprised me the other day by saying that he thought the College of Physicians was a dying organization. Certainly, the numerical facts do not justify such a conclusion. Whereas we were subscribing to 1,400 journals when I went on the Library Committee less than a decade ago, we are now subscribing to more than 2,000. The accessioned items in our Library have increased to nearly 200,000 and the College has constantly added to its collections of valuable historical material as well as to current material. Our assets have increased by two-thirds of a million dollars by raising new funds with which it was possible to increase our stack space by over 50 per cent and to modernize our present plant. During the past year we have safeguarded ourselves against a lack of parking facilities by the acquisition of the Erlanger Garage. What, then, led to this opinion?

I think the answer is to be found in the manner of participation of the Fellows of the College in its meetings and its affairs. The College cannot have true vigor if we own books but our Fellows do not read them, or if we hold lectures which our Fellows do not hear. I hope very much that during the next few years more and more of our Fellows will enter into the work of the College, and will let their desires be known regarding the acquisition of books, subscriptions to journals, section meetings, business meetings, and scientific programs. The pre-meeting dinners of the College offer an ideal opportunity to bring younger men, including residents and interns, to meetings of the College and to give them an opportunity to familiarize themselves with its facilities, to meet significant figures in scientific medicine, and to broaden their acquaintance among the best elements of the medical profession in the Philadelphia area.

On another occasion, I hope to be able to present to you a program of some of the objectives which we might wish to attain and to get your reaction as to their relative importance and priority. As is true of all institutions, we cannot stand still. A failure to move forward is synonymous with slipping back. During recent administrations the College has moved forward, and with your help I am sure we can look forward to further progress during the coming years.

[1] Remarks of the incoming President, College of Physicians of Philadelphia, 8 January 1958.

REPORT OF THE TREASURER FOR THE YEAR ENDED NOVEMBER 10, 1957

November 10, 1957

Assets

Cash in bank and on hand—general fund			$5,754.33
Maintenance and reserve fund			
Uninvested principal cash		$816.98	
Bonds		10,287.76	11,104.74
Assets held in trust funds (book values)			
Uninvested principal cash		10,626.57	
Unexpended income cash (restricted)		27,381.06	
Loan receivable—garage equipment		1,259.24	
Mortgage		47,250.00	
Real estate		154,421.10	
Bonds		277,079.30	
Preferred stocks		257,851.63	
Common stocks		354,869.10	1,130,738.00
Property			
Land—15–25 South Twenty-Second Street		95,000.00	
Building		1,420,747.93	
Furniture and fixtures		1.00	
		1,515,748.93	
Deposits on perpetual insurance policies		11,462.28	1,527,211.21
Total			$2,674,808.28

Funds

Unexpended income—general funds			
Library general account		$256.39	
Life membership account—uninvested portion		580.00	
Reserve for contingencies—uninvested portion		190.02	
Unexpended operating fund balances			
Current operating account	$3,647.93		
President's room	525.00		
Friends of library	20.00		
Books	230.49		
Rare books account	152.96		
Campaign expense account	175.95		
Portrait account	126.47		
Entertainment committee	51.30		
	4,930.10		
Less: Overexpended balance Harvey's "De Motu Cordis" Facsimile 1628 Edition	202.18	4,727.92	$5,754.33
Maintenance and reserve fund—principal			11,104.74
Unexpended income—trust funds (restricted)			
Discretionary common trust fund	24,376.22		
Legal common trust fund	527.18		
Trust funds not pooled	2,477.66	27,381.06	
Trust funds principal (book values)			
Discretionary common trust fund		1,017,058.07	

Legal common trust fund	24,097.94	
Trust funds not pooled	14,920.93	
Special account re: purchase money mortgage secured by North-east Corner 13th and Locust Streets property	47,250.00	
General endowment fund	30.00	1,130,738.00
Plant fund		1,527,211.21
Total		$2,674,808.28

Statement of Income and Expenses

November 11, 1956 to November 10, 1957

Income		
On investments, net of agent's fees		
Trust funds	$56,725.42	
Income funds, principal of which is not administered by the College of Physicians of Philadelphia	825.44	
Mortgage	2,189.53	$59,740.39
Contributions		
Fellows dues	55,265.00	
Life membership	1,925.00	
Entrance contributions	2,500.00	
Use of halls and projector	2,726.00	62,416.00
Library		28,935.23
Miscellaneous		2,510.85
Total income		153,602.47
Expenses		
Operating expenses		
Hall committee	28,616.29	
Office of the Secretary	6,101.62	
Office of the Treasurer	9,179.70	
Pensions	2,423.17	
Campaign expenses	175.00	
Publication committee	5,006.70	
College collections committee	3,245.33	
Books	1,583.11	
Entertainment committee	1,086.28	57,417.20
Library		
Salaries and payroll taxes	59,822.73	
Books, journals, supplies, etc.	24,490.61	84,313.34
Restricted trust funds		
Discretionary common trust fund	6,515.38	
Legal common trust fund	329.83	
Trust funds not pooled	394.79	7,240.00
Total expenses		148,970.54
Excess of income over expenses		$4,631.93

Receipts of special purpose funds from contributions and security investments not included in the above schedule were as follows during the fiscal year ended November 10, 1957:

Fund	Amount
Maintenance and reserve fund	$455.89
General endowment fund (voluntary subscriptions)	12,781.50
Friends of George E. Pfahler	150.00
College extension fund	671.50

ANNUAL SUMMARY STATEMENT

Endowment and Extension Funds of the College of Physicians of Philadelphia

I The General Endowment Fund

II The Restricted Endowment Funds

*III The College Extension Fund*p

I *General Endowment Fund*		
Total as of November 11, 1956 (Schedule A)		$328,065.83
Receipts 11-12-56 to 11-11-57		
1. Entrance Contributions	$2,625.00	
2. Gifts from Fellows (Annual appeal))	3,891.50	
3. Gifts and Bequests		
4. (All sources non-restricted) (Schedule B)	6,200.00	
5. Gifts from Book of Remembrance	480.00	
6. Amortization of Mortgage (13th & Locust Street)	2,250.00	
7. Building & Renovations Projects (Schedule C)	3,935.51	
8.	—0—	
9. Others	81.00	
	$19,463.01	
Less: Amount insufficient to purchase one unit credited to unit adjustment account	7.41	19,455.60
Total as of November 11, 1957		$347,521.43
II *Restricted Endowment Funds*		
Discretionary Common Trust Fund		
Total as of November 11, 1957		$511,157.40
Receipts 11-12-56 to 11-11-57 (Schedule D)		22,856.10
Total as of November 11, 1957		$534,013.50
Legal Common Trust Fund		$23,500.00
Separate Funds		$14,920.93
III *College Extension Fund*		
Receipts 11-12-56 to 11-11-57 (includes $668.34 in cash and the market value of 17 shares of Merck & Co., common stock donated during the year)		$1,212.48
Total Funds at book value, November 11, 1957		$921,168.34

Schedule A

Funds Transferred to the General Endowment Fund

Albert P. Brubaker Fund	$1,620.00
Samuel Clarkson Library Fund	2,890.00
College Endowment Fund	27,517.69
George E. deSchweinitz Fund	3,450.00
Carolyn Tyler & Arthur H. Lea Fund	53,710.00
Elizabeth S. Shippen Fund	5,500.00
William Weightman Memorial Fund	42,980.00

J. Harold Austin Fund	1,696.00
The Reserve Fund	133,056.64
Voluntary Contributions received before 11/10/56	8,577.68
Unexpended balances in the Building & Development Funds	47,067.16
Total November 11, 1956	$328,065.83

SCHEDULE B

Gifts and Bequests (All sources non-restricted)

John H. Gibbon Estate	$5,000.00
George E. Pfahler Estate	1,000.00
Kate Balentine Estate (In memory of Percy L. Balentine, M.D.)	200.00
Total November 11, 1957	$6,200.00

SCHEDULE C

Building and Renovation Projects

Payment of pledges to the former Building Fund	$1,375.00
Voluntary contributions to the Building and Development Funds (Annual appeal)	2,105.00
Additional interest Building & Development Funds	455.51
Total November 11, 1957	$3,935.51

SCHEDULE D

Receipts November 10, 1956 to November 11, 1957

Margaret L. Farley Library Fund	$4,995.78
Friends of George E. Pfahler Library Fund	142.20
Life Membership Fund	995.40
Mary Scott Newbold Lecture Fund	1,023.84
Pension Reserve Fund	469.26
Paul Judd Sartain Library of Ophthalmological Illustrations	1,237.14
Paul Judd Sartain Library Fund	$13,992.48
Total November 11, 1957	$22,856.10

JACOB H. VASTINE, 2nd, M.D.
Treasurer

Annual Report of The Library*

ADMINISTRATIVE

Introspection

PREVIOUS annual library reports have concerned themselves with expositions of basic policies governing certain areas of administration such as book and journal acquisition. Considerable attention has also been given to the problems peculiar to the privately supported learned society library. Now with the extensive remodelling and expansion project completed it seems logical to evaluate the quality and quantity of service being rendered by the library. Any effective long range planning must be predicated upon a realistic assessment of the present situation.

Book stacks. More than any other single factor, it was the crushing pressure of an ever-expanding collection which obligated the College to undertake the recent building program. The new stacks were ready for occupancy in the summer of 1956. During that summer and autumn the closing of the library for a week and the employment of extra help made it possible to spread the second, third, fourth, and fifth floors of stack into the adjoining space provided by the new stack.

The disposition of the Reserve Collection in February 1957 released about 486 shelves on the seventh floor of the old stacks. This together with another 648 shelves freed by the shifting of the dissertations to the sixth floor of the new stack provided the *Lebensraum* necessary to begin a shifting program on the seventh floor which will ultimately relieve the crowded conditions on both the sixth and seventh floors. It has also provided enough space to permit a future shift of the volumes in the "6" classification from the journal shelving on the first floor to the seventh floor where the remainder of the numerically classified material is housed.

At the close of the year presently under review, 182 shelves of pamphlets and books had been moved to new locations on the seventh floor. Another 151 shelves of material would have to be moved before the "6's" could start their journey to the seventh floor. Following this transfer another nine sections of material will have to be moved before a start can be made on the major part of the classified book stack which occupies the balance of seventh floor and all of sixth floor stack. Still untouched is the first floor of the old stack where the open space necessary for the beginning of a relocation project will have been provided by the movement of 324 shelves of "6's" to the top deck.

The actual manpower for this shifting is being provided by the Superintendent who is releasing part of the time of one member of the janitorial staff for this project. At the present rate of shifting, this program will require about two years' time.

Cataloging Department. Any discussion of unfinished business in this department must be based upon a report of the library administration prepared in September 1955. At that time an inventory of the backlog revealed 1,267 bound volumes and more than 1,525 pamphlets, bulletins, manuscripts, and documents. Major bequests from the Packard library, from Dr. Krumbhaar, the Twining anti-vaccination material, and about 300 old journal volumes from the Hahnemann Medical College remain as untouched as they were in 1955. More installments of Dr. Krumbhaar's library have been received since 1955 and although the Curator has prepared finding lists of this material, no entries have been prepared for the main card catalog. Considerable numbers of dissertations also await staff attention.

During the last two and one half years the library's one cataloger and her assistant have kept up with the newly published volumes being acquired by the library. However, virtually all of the older books and most of the

* 1 November 1956–31 October 1957.

pamphlets received have been added to the backlog. The accumulation was increased substantially during the stack shifting because of the discovery of items for which there was no record or for which the records were inaccurate. The 1955 report estimated that processing this arrearage would require at least one year's work by the present cataloging staff. It now seems evident that an additional full-time staff member could be expected to spend about two years to dispose of the backlog and probably three years to put this work on a current basis.

Sturgis Collection. Another area of the library's collections with an ever-growing accumulation of unprocessed material is the Department of Medical Art, affectionately known as the Sturgis collection. Prints of physicians and other illustrative materials are continually being received but none of it has been cataloged since 1948. Dr. Samuel B. Sturgis has a continuing interest in this undertaking and is willing to contribute his technical skill if clerical help could be found to work with him.

Exchange. The library continues to make duplicates available to medical librarians who can conduct their own scavenging operations in the basement. Large amounts of material were made available on this basis during the year to the Pennsylvania Hospital and to the China Medical Board. However, the library has not submitted a list of duplicates to the Medical Library Association Exchange since 1954. In order to maintain membership in good standing in the Exchange, lists must be offered at least once every two years. The library's inability to prepare lists has rendered it ineligible to request material offered on the lists issued by the Medical Library Association.

Serials Department. There are seasonal variations in the flow of material into the serials department and seasonal factors affecting the amount of material waiting for binding. For this reason the backlog has periods of waxing and waning but it never quite disappears. Approximately 1,400 individual items are entered upon the checking records each month. 1,611 volumes were sent out to the bindery during the year. Another 867 volumes were bound by the library's own staff. Piles of unfinished business quickly result whenever the delicate balance between available manpower and the routine pressure of work is upset by the processing of large shipments of gifts or the preparation of lists of duplicates.

March of this year was marked by the completion of the transfer of the serials' checking records to the visible index files which had been purchased more than a year earlier. By the time the transfer had been completed, the library was receiving more than 2,000 titles currently and it was painfully apparent that the index would have to be supplemented with an additional unit.

During the year the Superintendent remodelled two old tables for use in the Periodicals Room. These tables are used to hold indexes and bibliographies as well as current journals which require special binders. The most pressing need in this area is now the replacement of chairs which insult the eye and mortify the flesh.

Readers' Service Division. The library's short-comings in the service which it renders to its readers are not as easily measured as are the visible backlogs of the back stage operations. Readers who do not get what they want or telephone calls which are not answered do not appear as statistics. Whenever illness or unfilled vacancies occur in this area, assistance is recruited from other members of the staff and it is the regular work of the substitute which suffers. Because there is only one telephone at the circulation desk to handle two trunk lines it is often necessary to signal for help from the cataloging department when a second call requires attention.

A partial solution of this problem was brought into prospect at the end of the fiscal year when the financial situation permitted the ordering of a new charging desk which will allow the installation of two telephones on the desk. The new desk will also accommodate two persons to man this station during peak periods. The instruction of new personnel

should be greatly facilitated by the possibility of side-by-side teaching. To fully exploit the advantages of the new installation the Assistant Librarian in charge of Readers' Service should have enough time to be available during rush hours. The present incumbent of this position, however, is performing the dual role of Assistant Librarian and Director of the Medical Documentation Service. Because each is a full time job in its own right, it is to be hoped that the employment of a Director for the Service will become possible. This would release the Assistant Librarian for much of the work which is now being diverted to the cataloging department.

The end of the report year also witnessed the adoption of new circulation forms. These forms contain an interleaved carbon. The original copy becomes the library's record of what the reader has borrowed. The carbon copy is kept in a second file to show who has borrowed a particular volume. These forms will relieve the staff of the tedious chore of making second copies of all records.

An extension of the groups to whom the library may offer free borrowing privileges resulted from the concern of the library committee for graduate students in the biological sciences who are candidates for the M.S. or Ph.D. degree. Upon receiving sponsorship by a Fellow of the College these students are eligible to receive free borrowing privileges just as undergraduate medical students and hospital internes have been previously.

The end of the library's fiscal year made available figures which confirmed the suspicion that the library's photoreproduction services were being offered at considerably less than cost. A study of comparable rates charged by similar institutions proved that adjustments could be made in the charges without exceeding the prevailing prices.

Q. E. D. It is evident that the library has little basis for complacency concerning its operating efficiency or standards of service. It may fairly be said that with the tools at hand, as much is being done as can reasonably be expected. Nevertheless, those persons most intimately associated with the library, readers, Fellows, and staff alike are agreed that the library should be playing a more vital role in Philadelphia medicine. A research machine which costs as much to operate as does the College library should be utilized to the fullest extent.

Long range planning cannot be implemented until minimal levels of operational efficiency are achieved, but the importance of preserving the dream cannot be denied.

Library Staff

Seven members of the library's staff took advantage of the fact that the annual meeting of the Medical Library Association was held in New York City this year. They took particular pride in the enthusiatic reception accorded the Curator's paper on the history of the Association and they expressed a generous interest in the Librarian's election to the Board of Directors of the Association.

Miss Muriel Zeldis is serving as chairman of the Program Committee of the Philadelphia Regional Group of the Medical Library Association and Mr. Elliott H. Morse is a member of the Hospitality Committee of the Special Libraries Council of Philadelphia & Vicinity.

Miss Elizabeth Colabrese resigned in the middle of the year to accept an appointment to the staff of the library at the Eastern Psychiatric Institute. Following her resignation, this position was filled for brief periods by Mrs. Catherine F. Hanners and Mr. Lawrence Ferree. In September Miss Ella May Wallace was promoted from a library paging position to fill this post.

Shortly before the end of the year the library released Mrs. Lillian Ceci Pellicano the Assistant Cataloger, so that she could accept an appointment to the staff of Smith, Kline & French.

Benefactors

A list of the donors of books and other library materials appears in the statistical section of this report. A special grant was received from the Eberhard Foundation to enable the library to subscribe to Chemical Abstracts Service.

The library is pleased to report the following institutional subscriptions to the support of the library made under the Contribution Plan:

*Air-Shields Inc.
J. T. Baker Chemical Co.
Barnes, Dechert, Price, Myers & Rhoads
Bernstein & Bernstein
Borden Company—Chemical Division
Chew, Harvey, & Thomas
E. I. du Pont de Nemours. Haskell Laboratory
E. I. du Pont de Nemours. Lavoisier Laboratory
Eaton Laboratories
Freedman, Landy, & Lorry
Gray & Rogers
*La Wall & Harrisson
Lee Ramsdell & Co.
Lemmon Pharmacal Co.
MacAndrews & Forbes Company
*McNeil Laboratories, Inc.
*Merck Sharp & Dohme
*National Drug Company
Oxy-Catalyst, Inc.
Chas. Pfizer & Co., Inc.
*Quaker Chemical Products Corp.
Richter, Lord & Levy
Rohm & Haas Company
Samson Laboratories
*Smith, Kline & French Laboratories
E. R. Squibb & Sons
*Wallace Laboratories Division of Carter Products Inc.
Henry K. Wampole & Company, Inc.
Warner-Chilcott Laboratories
Wyanel Laboratories
*Wyeth Laboratories
Wyeth Laboratories—Marietta

E. H. M.

MEDICAL DOCUMENTATION SERVICE

The year 1957 was a busy one for the Medical Documentation Service of the College of Physicians of Philadelphia. Mrs. Jean Stevens skillfully managed the varied and increasing duties of Executive Secretary. The foreign language facility and subject background of Mr. Robert Blanken of the Department of Biochemistry, University of Pennsylvania proved valuable assets in scanning, translating and abstracting projects. Several new free-lance translators registered with the Service and a part-time typist was employed to meet the increasing work load.

* Institutions which have made contributions in excess of Contribution Plan standards.

A survey of M.D.S. activity during the year showed that 2,424 current references on 19 subjects were reported to clients of the scanning service, 117 literature searches and bibliography checks were made, 184 translations were completed, and 537 foreign and 310 English language articles were abstracted.

In addition to these regular services, M.D.S. contracted for two new special projects. The F. A. Davis Co., Medical Publishers, arranged for M.D.S. to provide consultant information service for subscribers to the Cyclopedia of Medicine, Surgery and Specialties. Biological Abstracts contracted for the translation of abstracts from the Russian abstracting journal *Referativniyi Zhurnal, Biologiia.*

On November 27, 1957 a symposium was held at the College to determine the future of M.D.S. Clients of the Service, members of the Library Committee and officers of the College were invited to a buffet luncheon to discuss possible ways of improving and expanding the Service. A short time before the date of the symposium, the New York Academy of Medicine announced the discontinuance of its Current References Service and several former subscribers to that Service asked to be represented.

Several institutional clients reported on the value of M.D.S. to their research programs and helpful suggestions were made for more widely publicizing the Service. Participants in the symposium advised the library administration to revise the fee schedule to provide an income sufficient to eliminate the operating deficit which was threatening the continuation of the service.

The library administration and M.D.S. staff were extremely gratified by the interest shown by the clients. A revised fee scale was established which will more nearly meet the costs of operation and we look forward to extending M.D.S. to an increasing number of individuals and organizations engaged in medical research.

J. A. W.

HISTORICAL

GENERAL

The library's historical department (faculty of one) inevitably reviews the past year's activities with mixed emotions. Considerable progress was made, for instance, in transferring the rare-book material from the old stacks to the rare-book floor of the new—but the job was not completed. A list of the library's holdings of editions of the works of Nicholas Culpeper was made available to the compilers of a bibliography of Culpeper editions; but reasonably expected assistance to several other bibliographic projects is still pending, awaiting sufficient time for the detailed studies involved. The library's cataloguer, in consultation with the curator, revised the cumbersome subject-heading scheme for the historical material; but long-continued lack of secondary help in the cataloguing department prevented revision of the hundreds of cards removed from the catalogue for the purpose, and that are still out of the catalogue. Joy over new acquisitions was clouded by the knowledge that, owing to this same difficulty, the new acquisitions must join many hundreds of earlier Galateas awaiting the attention of a Pygmalion. The selection of acquisitions for purchase was itself dominated, as always, not only by the paucity of funds for this purpose but by the time required for checking innumerable booksellers' catalogues against the card catalogue, and then perhaps for soliciting funds not routinely available. Unlike collections in which acquisition is the primary concern, ours has, of course, multiple time-consuming requirements to meet, and the amount of time devoted to determining suitable candidates for acquisition cannot usefully dominate the temporal budget—particularly so, one might think, when conditions prevent the acquisitions from assisting in meeting the numerous and varied demands made on the collections.

Having thus conscientiously—if somewhat more briefly than usual—hinted once again that adequate housekeeping of one of the world's great medico-historical collections requires a larger staff than ours can boast, we proceed to pleasanter matters.

SOME ACQUISITIONS*

OF EUROPEAN ORIGIN:

Bailey [Baily, Bayly], Walter. A Briefe Discours of Certain Baths or Medicinall Waters in the Countie of Warwicke neere unto a Village Called Newnam Regis. [London], 1587. [S.T.C. 1192] [Bound with the Tonstall items below]. [In the year preceding the publication of this balneological treatise, Dr. Bailey had published a *Briefe Treatise Touching the Preservation of the Eie Sight* (a later edition is in the library), which Dr. Burton Chance has characterized as "the first separate work on ophthalmology published in England . . ." "Bailey", says Dr. Chance, "was physician to Queen Elizabeth who, while doubting the value of wine for bathing the eye, recommended ale to strengthen the sight". In the present treatise the Royal physician seems to have attained a soberer scientific stance, for Sir D'Arcy Power has written, "His treatise on the baths at Newnham Regis proved him to have been possessed by the spirit of his age, so that if he had lived at a later time he would have been a pharmacologist and a scientific physician with a strong leaning to the chemical side of medicine."]

Haslam, John. Observations on Madness and Melancholy. 2d ed. London, 1809. [Ownership inscription of Nathaniel Chapman]. *Gift of Friends Hospital, through Theo. L. Dehne, M.D., Superintendent.*

Lind, James. Essai sur les Maladies des Européens dans les Pays Chauds. Paris, 1785. *Gift of Friends Hospital, through Theo. L. Dehne, M.D., Superintendent.*

Madden, R. R. Travels in Turkey, Egypt, Nubia, Palestine in 1824, 1825, 1826, 1827. 2 vols. London, 1829. [Though he practiced as a surgeon for a while, and was elected a Fellow

* Further acquisitions are described in our *Fugitive Leaves from the Library*, N.S., No. 17, November, 1957.

of the Royal College of Surgeons, Madden is chiefly remembered as a government administrator who labored zealously on behalf of the natives of the various colonial possessions to which he was assigned.] *Gift of Mrs. Ethel C. Elkins Lau.*

Paracelsus. Die groote Chirurgie. Antwerp, 1556. [Sudhoff I, no. 35.] [There appears to be only one other recorded copy of this edition of Paracelsus' principal work, that in the University of Amsterdam. The purchase was stimulated largely by the Hahemann Medical College's recent deposit of its Hering Paracelsus Collection in our library, announced in last year's report.]

Parchappe, J. B. M. Traité Théorique et Pratique de la Folie. Paris, 1841. *Gift of Friends Hospital, through Theo. L. Dehne, M.D., Superintendent.*

Porzio, Simone. Tratato de Colori degl'Occhi. Florence, 1551. [The original edition, in Latin, of this Pisan professor's little book on the colors and structure of the eye was published in the preceding year, and is not exceptionally rare (a copy is in our library); we did not find the Italian edition listed in the major catalogues, from Haller on.]

Tonstall, George. A New-Years-Gift for Doctor Witty; or the Dissector Anatomized: Which Is a Reply to the Discourse Intituled, *An Answer to All That Doctor Tonstall Has Writ, or Shall Hereafter Write, against Scarbrough Spaw.* London, 1672. [Wing T 1888] [Bound with the Walter Bailey item above and the Tonstall item just below]

Tonstall, George. Scarbrough Spaw Spagyrically Anatomized. London, 1670. [Wing T 1889] [Bound with the Bailey and Tonstall items above] [Partial documentation of a bitter controversy over the merits of the mineral waters of Scarborough that engaged the attention of the British medical profession for a number of years in the latter half of the 17th century. The "Doctor Witty" concerned was Robert Wittie, later an Honorary Fellow of the Royal College of Physicians. The library has his translation of James Primrose's *Popular Errours* (London, 1651), but none (at least catalogued) of his several pamphlets dealing with this controversy.]

Of American Origin

Manuscripts

Bitner, Abraham. Note's[sic] taken from the Philadelphia, Almshouse. by A. Bitner Novr. 1824. vol. 1. [Beginning at the other end of the volume: Notes on the lectures of Nathaniel Chapman, taken in 1825] *Gift of Joseph Appleyard, M.D.* [Bitner, of Lancaster, Pa., was a member of the second class to be graduated from the Jefferson Medical College, in 1827. The volume is not quite equally divided between the notes on Chapman and the notes taken at the Philadelphia Almshouse (now the Philadelphia General Hospital). In view of the numerous volumes of student notes on Chapman's lectures, the hospital notes will probably be found the more rewarding. These give us case histories, with the prescribed treatment, of named patients, along with notes on the demonstrations by Chapman, William Gibson, and John Redman Coxe. As a doodler, young Mr. Bitner ranks with the more provocative of the clan. His thoughts are expressed sometimes in English, now in Pennsylvania Dutch; again, in a sketch of a formidably constructed young woman over whose head appears the word *Commune.* The two languages come together after a fashion in the cynical observation that heads his notes from the Almshouse: "I was well, wished to better, took medicine & died." Of the later Dr. Bitner, Dr. Appleyard, secretary-treasurer of the Lancaster City and County Medical Society, was able to learn only that he was a charter member of the Society (1844), and that its minutes contain a Resolution on his death, which occurred 31 Oct. 1854.]

Dorland, William Alexander Newman (1864–1956). Scrapbook, vol. 8. *Gift of Mrs. W. A. N. Dorland.* [Elected a Fellow of the College in 1897, Dr. Dorland, whose name is familiar to all users of American medical dictionaries, left Philadelphia somewhat over a decade later but

retained his fellowship in the College, and a watch on its activities, until his death. Over the years, there would come to us from time to time an additional scrapbook containing many sorts of interesting records of his activities. This final volume brings to a regretted close a rare treasure-house of letters and documents.]

Garrison, Fielding Hudson (1870–1935). [A sheaf of unpublished letters written to Burton Chance, M.D.] *Gift of Dr. Chance.* [These letters, characteristically reflecting many sides of the personality of this great American medical historian, provide a valuable addendum to the "Life and Letters" published by S. R. Kagan in 1938.]

Jackson, David (1747?–1801). [Ms. letter to Dr. John Kuhn, of Lancaster, Pa., 1800] *Gift of Joseph Appleyard, M.D.* [Jackson, "physician, apothecary, patriot", was the father of Samuel Jackson (1787–1872), one of the most popular of Philadelphia's medical teachers in the 19th century. With the letter is a note to Dr. Kuhn, dated 1806, from Samuel Jackson's brother David, who carried on the family drug business after the father's death.]

Lyon, Bethuel B. Vincent (1880–1953). [Ms. notes on the lectures of Thomas R. Boggs, on clinical microscopy, at Johns Hopkins University, 1905/06] [Boggs was characterized by Osler as a "jewel". Lyon, a Fellow of the College, is remembered as one of the great American gastroenterologists and internists. The B. B. Vincent Lyon Collection (in its own illuminated cabinet) of lantern slides illustrating duodenal tube drainage of the biliary tract is one of the features of the College's Mütter Museum.]

Sartain, Paul Judd (1861–1944). [European diaries. 5 vols., 1875, 1887–89.] *Gift of the Sartain Estate.* [This cultured ophthalmologist and Fellow of the College bequeathed to the library a fund for the purchase of ophthalmological illustrations; and following his death we received four of his student notebooks and a case-book (1883–85). The newly received diaries mingle notes on his professional studies and general travel observations in several countries.]

Thomson, William (1833–1907). [Case-books, Vols. 1, 2, 4, 7, 9–11, 13–20. 1869–90.] *Gift of Burton Chance, M.D.* [Thomson's work in experimental optics and ophthalmic surgery won for him a distinguished reputation. He was elected a Fellow of the College in 1869. A splendid portrait of him by the celebrated Thomas Eakins graces the College's Thomson Hall, which was named for him. The obvious historical value of these case-books arouses the hope that the set may somehow be completed by the restoration to it of vols. 3, 5, 6, 8, and 12.]

Books

Coxe, John Redman. An Inquiry into the Claims of Doctor William Harvey . . . Phila., 1834. *Gift of Mrs. Catharine Pierce.* [An association copy: it contains a presentation inscription and a letter from the author to Thomas Tickell Hewson, President of the College, 1835–1848.]

[*Ruschenberger, W. S. W.*] Three Years in the Pacific. Phila., 1834. *Gift of the Friends Hospital, through Theo. L. Dehne, M.D., Superintendent.* [In last year's report we noted the acquisition of three manuscripts stemming from this widely traveled naval surgeon and quondam President of the College. It was also observed at that time that the library had none of the three highly regarded books on his voyages published by Dr. Ruschenberger. While that report was still in press, there came a gracious invitation to select from the historical books in the Friends Hospital any that would augment our historical collections. The first book in that category to present itself was this one. During the long voyage of the present report through the press, we shall be on the alert, naturally, for a similarly fortuitous opportunity to acquire the remaining two books: *A Voyage around the World*, and *Notes and Commentaries during Voyages to Brazil and China.*

Schüssler, W. H. Abridged Therapeutics. 9th ed. New York, 1884. *Gift of Joseph W. Post, M.D.* [A once enormously popular work

by the German founder of a cult called "biochemical therapeutics".]

Tobler, John. The Pennsylvania Town and Country-man's Almanack, for the Year of our Lord 1756. Germantown, Christopher Sower, jr, [1755]. *Gift of Burton Chance, M.D.* [A rare imprint of a type of publication useful for its information on folk medicine.]

EXHIBITS

Each of the five meetings of the College's Section on Medical History held in the period covered by this report was provided with an historical exhibit illustrative of the subjects discussed. A total of some 14 subjects permitted a revelatory glimpse of the length and breadth of the library's historical collections. In addition, there were four special exhibits: one commemorating the 60th anniversary of the Philadelphia Pediatric Society; another, of rare herbals, prepared in collaboration with Mrs. Henry Cadwalader for the annual meeting of the Herb Society of America, which held some of its sessions at the College; a third, provided by our Fellow Dr. Clifford B. Farr, of the Institute of the Pennsylvania Hospital, displayed chiefly a large number of historically valuable letters written to Dr. Thomas S. Kirkbride by prominent 19th century psychiatrists; and fourth, a William Harvey exhibit, commemorating the tercentenary of the death of the great physiologist. A hoped-for improvement of the display facilities unfortunately was not achieved.

FUGITIVE LEAVES

Nine numbers (N.S., Nos. 8–16) of the *Fugitive Leaves* were issued during the year under review. Two of them brought to conclusion the inventory of the Hering Paracelsus Collection that was referred to at this point in the report for the preceding year. No. 10 published a letter from a Lancaster, Pa., medical student named J. H. Kurtz giving his impressions of the medical instruction being offered at the University of Pennsylvania and the Jefferson Medical College in 1834. The letter was reprinted, with our permission, in the May, 1957, number of the *Bulletin of the Lancaster City and County Medical Society.* Nos. 11–15 make available author and addressee indexes to the library's valuable and frequently used Gilbert Collection of manuscript letters and miscellaneous documents. No. 16 described briefly the Israel Bram Collection of replies to a questionnaire on sleeping habits, and provides an index to the 150-odd distinguished persons who replied to Dr. Bram's questionnaire.

IN PRINT

"William Harvey, Weir Mitchell, and the College of Physicians of Philadelphia", an article prepared by the curator at the request of the Editor of the *Journal of the History of Medicine and Allied Sciences*, appeared in The William Harvey Issue (April, 1957) of that journal. It chiefly re-directed attention to one of our copies (at one time in the possession of Weir Mitchell) of Harvey's *De Generatione*, London, 1651, which seems to be the only known copy of a Harvey edition containing evidence that it had been a presentation copy from the author.

The July, 1957, issue of the *Bulletin of the Medical Library Association* contained an article by the curator entitled, "Snapshot of the Medical Librarian as Historian and Bibliographer, to 1947"; and the October, 1957, number of the same journal, two further pieces: "A Salute to Some Milestones, Detours, and Dead-ends in the History of the Association", which had been read at the Annual Meeting of the Association, held in New York, in May; and "Thomas E. Keys", a brief sketch of the Mayo Clinic's Librarian, who had become the Association's President at that meeting. None of these assignments was undertaken as a result of curatorial initiative; but they may be thought to represent another legitimate facet of the work of a live historical apparatus that adds to the liens on the temporal budget.

W. B. McD., 2d

STATISTICAL SUMMARY

Inventory

Accessioned items:	1957		1956	
Accessioned items[1]				
Incunabula[2]	419		419	
Manuscripts and typescripts	924		879	
General	191,066		187,036	
Accessioned pamphlets	4,380		4,345	
		196,789[3]		192,679
Unaccessioned items[1]				
Reports	28,837		28,579	
Periodicals "reserve"	0[4]		10,935	
Theses	58,667		58,340	
Pamphlets and reprints	231,328		231,094	
		318,832		328,948
Portraits[5]	101,333		98,777	

Current Serials

	Subscription	*Gift*	*Exchange*	*Total*
U. S. A.	344	391	67	802
Western European Continent	639	47	78	764
Latin America and West Indies	20	80	82	182
United Kingdom and Eire	125	25	23	173
Canada	9	18	9	36
Eastern European Continent	19	22	17	58
Asia (including Japan)	18	43	42	103
Africa	3	2	14	19
Pacific (including Australasia)	3	8	9	20
United Nations	12	0	0	12
Grand Total: 1957	1,192	636	341	2,169
Grand Total: 1956	1,182	576	358	2,116

New titles: A total of 127 serials was added in 1956–57. 44 of these were purchased; 83 received in exchange or gratis.

Separate Issues received, checked in on the cards, and shelved totaled 17,764. In addition, thousands of dupli-

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[1] Accessioned items in this library comprise the total number of bound volumes and such unbound pamphlets as have been catalogued as separate bibliographical units regardless of their size.

There remain many thousands of unaccessioned pamphlets awaiting accessioning and cataloguing. A true quantitative and qualitative picture of the library's holdings cannot be presented until this wealth of neglected material has been processed and duly registered in our 'accessioned', or 'volume', count.

[2] The library owns 421 incunabula but there are two cases of two bound together, reducing the number of accessioned items.

[3] Included in this figure are the following collections which are on permanent deposit in the library: Gross Library, 3,972 accessioned and 4 unaccessioned items; Parry Library of the Obstetrical Society of Philadelphia, 217; Mütter Museum, 200 (Mütter Museum books may not be removed from the College building).

[4] The "Reserve" collection was disposed of during the year. No attempt has been made to count the "new Reserve" collection which consists of issues of about 75 journal titles from 1950 to date.

[5] Including 123 oil, and 268 other, framed portraits in the care of the Committee on College Collections. The count of portraits represents the number of entries on the cards in the portrait catalogue. The entries represent, in turn, both loose portraits and those in books, many of them, of course, being merely different reproductions of a single original.

cate issues were received as usual. No attempt was made to count those held merely for exchange or other use.

Visitors in the Norris Room for the year totaled 3,223.

Readers' Use of the Library

Library Hours. The library was open, during the academic year, from 9:30 to 9:30 on Mondays and Wednesdays; from 9:30 to 5:30 on the other weekdays. During the latter half of June, in July, August, and the first half of September the library was open from 1 to 9:30 on Tuesdays; from 9 to 5 on the other weekdays except Saturdays, when it was closed. The following legal holidays were observed: Thanksgiving, Christmas and New Year's, Memorial, Independence, and Labor Days.

Visitors:

	Totals
1957:	11,479
1956:	11,500

Circulation:

	Totals:	*Intra-mural*[6]	*Extra-mural*[7]	*Books*	*Journals*
1957:	50,393	38,085	12,308	10,469	39,924
1956:	37,397	26,088	11,309	6,934	30,463

Inter-library loans: The library sent 6,926 (1956: 4,714) volumes on inter-library loan to 170 (1956: 187) libraries in 31 (1956: 27) States, Washington, D. C. and Canada and has borrowed 15, (1956: 5) volumes from 10 (1956: 3) libraries.

Photostats and Cormac Sheets: 4,432 Photostat and Cormac prints were furnished on request (1956: 4,648).

[6] The number of volumes "consulted in the library" includes only those supplied on demand. Readers have access to the bound volumes of periodicals and reference works kept on the shelves in the Reading Room; the Fellows, and occasionally others, by special permission, have access to the book-stacks. There are, therefore, many volumes consulted of which no accurate record can be kept.

[7] This figure includes 1,118 unbound current issues circulated from the Periodicals Room.

Acquisitions and Accessions

Accessioned Acquisitions:

1957: 4,110 volumes (2,364 by purchase; 1,367 by gift; 379 by exchange). (*Books*: 1,413; *Periodicals*: 2,662; 35 *pamphlets*).

1956: 3,137 volumes (1,993 by purchase; 937 by gift; 195 by exchange). (*Books*: 1,105; *Periodicals*: 2,029; 12 *pamphlets*).

Non-accessioned Acquisitions:[8]

1957: 258 Reports (1956: 289)
327 Theses (1956: 512)
259 Miscellaneous items (1956: 250)

Donations

The donors for the past year number 154 (1956: 208). The library is indebted for large gifts of books, pamphlets, and unbound periodicals to the following donors: Drs. S. Bellet, B. Chance; F. A. Davis Co.; Hahnemann Medical College Library; Jefferson Medical College Library; Drs. R. A. Kern, E. B. Krumbhaar; Lea & Febiger; J. B. Lippincott Co.; W. B. Saunders Co.; Smith, Kline & French Laboratories; South African Institute for Medical Research; Dr. I. J. Wolman; Wyeth Laboratories.

Various publishing houses, among the large group of corporate donors, have presented volumes as follows: F. A. Davis Co., 9; Lea & Febiger, 19; J. B. Lippincott Co., 30; W. B. Saunders Co., 68.

Other individual donors were as follows: Prof. J. Q. Anderson; Drs. J. Appleyard, J. Aranalde Rode, W. Blakemore, C. S. Bluemel, M. H. Book, C. P. Brown, D. L. Cowan, D. M. Davis, T. L. Dehne; Mrs. W. A. N. Dorland; Dr. G. Duncan; Dr. P. Drant Estate: Dr. A. G. Fewell; Miss C. R. Flick; Mrs. R. F. Gerlach; Dr. B. L. Gordon; Miss A. Hartshorne; Drs. C. L. Jackson, A. L. Katcher, G. P. Keefer; Miss M. B. Kirkbride; Drs. D. W. Kramer, C. H. LaClair, Jr.; Mrs. E. C. Elkins Lau; Dr. W. G. Leaman; Mr. W. R. LeFanu; Drs. F. Lewis, M. M. Lieber; Mr. W. B. McDaniel, 2d; Dr. L. C. McGee; Mrs. B. M. Mitchell; Mr. E. H. Morse; Dr. C. Mucklé; Mr. F. N. L. Poynter; Prof. P. P. Pupo; Drs. J. E. Rhoads, F. B. Rogers, J. B. Rudolphy; Sartain Estate; Drs. J. P. Schaeffer, H. G. Scheie, D. M. de Silva, W. E. Siri, E. H. Spaulding, J. A. Sterling, C. Urbach, J. I. Waring, J. P. Warbasse, F. D. Weidman; Mr. D. H. Wenrich; Drs. A. H. Whittaker, P. F. Williams.

[8] As usual, not all the pamphlets, theses, and numbers of various journals listed as received had been checked for keeping or discard at the close of the library year.

The *Transactions & Studies* was sent, either in exchange or as gift, to 443 organizations.

The library received a number of journal issues through gifts and supplied duplicate journals to other libraries through a variety of channels.

Theses and dissertations to the number of 327 have been received on exchange from the following European schools of medicine: Universities of Basel, Bern, Copenhagen, Erlangen, Lausanne, Louvain, Lund, Paris, Uppsala.

Work of the Cataloguers

	1957	*1956*
Accessioned items catalogued or recatalogued	919	902
Unaccessioned items and Fellows' reprints catalogued by author or by author and subject	372	392

The Staff[9]

Librarian
Elliott H. Morse

Assistant Librarian
Readers' Service Division
Josephine A. Walsh
Readers' Service
Division Assistant
Ella May Wallace
Serials Librarian
Muriel Zeldis

Assistant Librarian
Preparation Division
H. Muriel Hodge
Assistant Cataloger
Zena Babych

Serials Assistant
Dorothy Minton

Secretary and Preparations Assistant
Mrs. Kathryn E. Miragliotta

Curator of the Library's Historical Collections
W. B. McDaniel, 2d

Medical Documentation Service
Mrs. Jean C. Stevens, Executive Secretary
Pages
Robert Glass
Janice Greene
Betty Jones
Catherine Ledwell

Approved:
Burton Chance, M.D.
Chairman

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[9] Library staff list as of March 1, 1958.

Annual Report of the Committee on the Mütter Museum and College Collections

THE Mütter Museum of the College of Physicians continues to attract visitors from the various schools and colleges in and around Philadelphia, besides many students and professional individuals from other states and foreign countries. It is open daily except Saturdays and Sundays, from 9.30 A.M. to 1 P.M. and from 2 P.M. to 4.30 P.M. The curator is also in attendance on the Stated Meeting Nights of the College until 8.30 P.M.

This year many attending special meetings at the College took the opportunity to visit the Museum for the first time. As in former years large classes from the Franklin School of Science and Arts and Girls' High School visited the Museum, and classes from Hahnemann Medical College, Temple University School of Medicine and Woman's Medical College seemed to find their visits rewarding. The Montgomery Hospital in Norristown is now making it a practice to send classes of student nurses to the Museum each year. The number of visitors this year was 1882.

Certain historical objects housed in the Museum, but belonging to College Collections, served to illustrate a short talk on Mercy Museums given on a television program by Professor Welch from the Philadelphia College of Pharmacy.

Dr. Samuel X Radbill's class in Pediatrics made their usual tour of the Museum, inspecting early bloodletting instruments, stethoscopes, infant feeding boats and other historical instruments.

More than one hundred articles have now been written on Museum subjects, and while, as yet, no one seems inclined to undertake assembling them in book form, it is rewarding, at times, to find one or more articles reprinted in some other periodical. The article on the deaf mute, Laura Bridgman, appeared in the September issue of The Pennsylvania Medical Journal.

The following gifts presented during the year are now permanent exhibits in the Museum:

Presented by the will of Dr. George E. Pfahler:

Crooks Tube used by Prof. Conrad Roentgen in 1895. (Replica made by Dr. Harvey Rentschler. Tube holder used in 1896).

First Focal x-ray tube used at the Medico Chi Hospital in 1896 by Dr. Pfahler.

Universal Coolidge Therapy tube used by Dr. Pfahler from 1910 to 1950.

Gas Radiographic tube used by Dr. Pfahler from 1910 to 1925.

First Superficial Therapy tube designed by Dr. Piffard of New York and used in 1905 by Dr. Pfahler.

Presented by Dr. Lewis C. Scheffey:

Obstetrical forceps with ivory handles on which is engraved, "Dr. James C. Bloomfield from Dr. William E. Ashton for the best examination on Obstetrics and Gynecology, 1888."

Mrs. Ella N. Wade was reappointed curator for the year 1957–58.

The College Collections

During the year the following portraits were restored by Mr. Frank Ireland: Charles W. Burr, Samuel D. Gross, Benjamin Duffield, William Harvey and Thomas S. Kirkbride. The renovation of the portrait of Samuel D. Gross disclosed the name of the artist and a date, namely, T. Dimino, Rome 1909. As Dr. Gross died in 1884, this portrait must be a copy of another.

Again the College was generously remembered by friends and many new items were added to the College Collections.

Dr. Robert F. Norris contributed a Brodie-Russell-Boggs coagulometer, a planimeter and a combined sphygmobolometer and sphygmomanometer.

An ivory and gold stethoscope, dated 1883, was presented by *Dr. Theodore F. Bach*, and the *Philadelphia Pediatric Society* gave a bronze medal of Clemens Pirquet.

An unusual massage apparatus, named Dr. Macaura's Blood Circulator was presented by *Mr. K. Hobart Roatch*, and three neat medicine cases containing pills and powders, that formerly belonged to Dr. Harriet Judd Sartain, were presented by *Mrs. Arthur Meltzer* from the estate of *Miss Harriet Sartain*.

One College Night *Dr. Henry V. Grahn* offered a Civil War emblem that had belonged to Dr. David Hayes Agnew, which he, in turn, had received from a Mrs. Montgomery.

Dr. Burton Chance presented a magnet that he has used since 1894 to remove foreign objects from the eye.

Mrs. George E. Pfahler presented, from Dr. Pfahler's estate, a medal of J. Belot and a bronzed plaster bust of Dr. George E. Pfahler, done by his secretary, Marie F. Carley in 1942.

The Wyeth Laboratories had replicas made of an original Laennec stethoscope in the Mütter Museum, and through *Dr. Robert S. Warner*, generously presented one of them to the College.

An interesting and valuable album on meningitis prepared by *Dr. D. Franklin Royer* for the Annual Meeting of the American Medical Association held in Atlantic City about 1906, was the gift of *Dr. Royer*.

Dr. Eunice Stockwell presented a small microscope of unknown date.

Dr. J. Monroe Thorington is one of our most generous donors, and this year he brought us the following items from Europe: wax votive offerings from small shops near the church at Vigo, Galicia, Spain; wax votives offered to St. Anthony from Oviedo, Asturia, Spain; metal votive offerings of St. Anthony of Padua, made in Naples from ancient dies; a St. Anthony medal; a group of St. James talismans and a pharmacy jar from Madrid, Spain.

Dr. Thorington also presented an old pair of spectacles, a magnifying glass for eye examination, venesection knives formerly belonging to Caspar Rehn (1780–1854) of Philadelphia, an American ambulance pin (France 1914), schematic eye for instruction in retinoscopy designed by Dr. James Thorington (1858–1944), and an opium set obtained from San Francisco.

Mrs. Ella N. Wade was reappointed custodian of College Collections for the year 1957–58.

THEODORE F. BACH, M.D., *Chairman*

Memoir of Frank Crozer Knowles (1881–1957)*

By EDWARD F. CORSON, M.D.

FRANK CROZER KNOWLES, a Fellow of this College for nearly fifty years, was born in Philadelphia, January 26th, 1881. The son of Gustavus Warfield and Emma Crozer Knowles, he was the next to youngest in a family of nine children, two of whom survived him.

After graduating from the William Penn Charter School in 1898, Dr. Knowles entered the Medical School of The University of Pennsylvania directly, graduating at the age of 21. While a student he was a member of the William Pepper Medical Society and the Delta Kappa Epsilon and Alpha Kappa Kappa fraternities. Soon after beginning an internship at the Presbyterian Hospital he had the misfortune to contract diphtheria and had barely recovered from that disease when he fell a victim to typhoid fever, then epidemic in this city. After a prolonged convalescence he spent a year abroad, during which period he regained his health and extended his medical education.

On his return to this country he attended various out-patient dispensaries in Philadelphia with the view of regaining the training lost by his short-lived internship. Ophthalmology, urology and dermatology were considered in turn as specialties appealing to him, but soon he decided on the last-named branch of medicine and gave it his entire attention. He formed numerous hospital connections and profited by his association with an outstanding group of dermatologists-Duhring, Stelwagon, Hartzell, Van Harlingen and Davis. He soon gained the confidence of his chiefs and cared for the summer practices of most of these eminent dermatologists. His principal early hospital connections were the Philadelphia General, University of Pennsylvania, Howard, Pennsylvania and Children's, but in consultant rank he served numerous other institutions. For ten years he was Clinical Professor of Dermatology at the Women's Medical College. He was Dermatologist to the Pennsylvania and Presbyterian Hospitals. Ascending through various grades he became Assistant Professor of Dermatology at his *Alma Mater*. A frequent contributor to dermatologic literature, his subjects were well-chosen, timely topics, useful, thoroughly prepared and, when spoken, well delivered. His text-book on *Diseases of The Skin* was well-received by practitioners and students and four editions were published.

Soon after the United States entered World War I, Dr. Knowles joined the Pennsylvania Hospital Unit, U. S. Base Hospital No. 10, among the first of such organizations to be sent overseas. In the English service it functioned as British Hospital No. 16. There Dr. Knowles was Dermatologist and occasionally, Roentgenologist. Later he was appointed Dermatological Consultant to the A.E.F. and made journeys of inspection to various other hospitals and to combat divisions.

On returning to this country, after 23 months overseas, he was ordered to Washington in 1919 to write the Section on Dermatology in the permanent Medical War Records. He held the rank of Colonel in the Medical Officers Reserve Corps. He was an early member of the American Academy of Dermatology and Syphilology and in 1939 was elected President of the American Dermatological Association, of which he was later made an Honorary Member.

Jefferson Medical College in 1920 elected Dr. Knowles to the Chair of Dermatology, in which capacity he served for twenty-seven years. In 1951 that college conferred upon him the Honorary Degree of Doctor of Science.

* Read before the College of Physicians of Philadelphia, 11 December 1957. Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

So much for the professional side of the subject, the part open to the students, patients and his colleagues. To his more intimate friends he presented numerous other facets. With a well-proportioned athletic figure he was a powerful long distance swimmer and a rower in his early days, tapering off through tennis to golf, the latter indulged in up to the age of 70. He was a member of the Merion Cricket and Golf Clubs and the University Club of Philadelphia. He was a zealous collector of certain types of antiques. He acquired outstanding examples of Queen Anne and Early Georgian furniture and splendid specimens of Chinese porcelain. Some of these objects are said to be practically unique.

He was modest and conservative, a loyal friend and a kindly gentleman. Dr. Knowles died in Jefferson Hospital on January 9th, 1957, after a prolonged illness.

Memoir of John Byers Roxby (1871–1957)*

By JOHN A. KOLMER, M.D., Dr. P. H.

DOCTOR JOHN BYERS ROXBY, son of John Crawford and Mary Cather Roxby, was born on May 18, 1871 in Shenandoah, Pennsylvania and died in his 86th year in Philadelphia on March 18, 1957. Following graduation from Shenandoah High School in 1888, he entered the Millersville State Normal School, where the principal stated, "Your attitude toward the work is that of an earnest learner; this will bring success". He was greatly disappointed when a third severe attack of rheumatic fever necessitated his withdrawal from college, producing enough cardiac damage that when he became a medical student an instructor in physical diagnosis advised him that it would be useless for him to pursue the study of medicine. A zeal for education motivated him in his personal and family life thereafter.

He went to work in a department store when his family moved to Philadelphia in 1889, but in 1892 he began to study under a preceptor, Dr. George H. Richardson, 1724 Diamond Street. Other preceptees of this kindly physician were Dr. Arthur C. Morgan and Dr. Brooker Mills, who also became members of the major faculty of the Temple University School of Medicine.

Dr Roxby matriculated in the Medico-Chirurgical College in 1893. When graduated with honors in 1896 he was valedictorian of his class. In the following year he was appointed demonstrator in anatomy at his *alma mater* and in 1899, chief demonstrator and instructor. Becoming a master in the art of gross dissection, many of his preparations were selected by his chief, Dr. Heissler, as models for the artist who illustrated Piersol's "Textbook of Anatomy." Perhaps his best contribution to the field of anatomy was one of the first gross dissections of the autonomic nervous supply to the adrenal gland. His love of teaching was evident in the voluntary evening quiz sections in anatomy which were attended by scores of students from various local medical schools.

He resigned his position in 1902 to engage in general practice in the village of Warriors Mark in central Pennsylvania. In 1903 Dr. Roxby was appointed professor of anatomy in the Temple University School of Medicine, which was then an evening school. His laboratory was in the loft of a stable behind the old Samaritan Hospital, now the Temple University Hospital. In 1903–1904 he was also a lecturer in neuro-anatomy at the Woman's Medical College of Pennsylvania, and in 1905 served as professor of anatomy in the Philadelphia Dental College which, in 1907, became the School of Dentistry of Temple University. He was partially instrumental in persuading Rev. Russell H. Conwell to transform the Temple University School of Medicine into a day school and it was he who made the motion in the faculty that the night curriculum be abandoned. During the summer of 1907 he studied at the University of Edinburgh in the laboratory of the distinguished author of Cunningham's "Textbook of Anatomy", examining specimens prepared for the "Edinburgh Atlas of Anatomy".

While teaching at night, Dr. Roxby had established a general practice in Swarthmore. In 1914 he resigned his position to devote himself exclusively to private practice. For a time he practiced in Loganton, near Williamsport, Pennsylvania, driving a horse and buggy to attend patients in remote mountain locations. He soon returned to Swarthmore, where he continued his practice. In 1925, however, he returned to the Temple University School of Medicine as full time professor and head of the department of anatomy which he held until retirement in 1944 as professor emeritus of

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

anatomy and "one of the foundation stones of the Temple University Medical Center" (Dean Parkinson). It was his privilege to design the present laboratory of anatomy and its equipment. Among his students during this period were several sons and daughters of physicians whom he had taught during his earlier tenure. From 1938 to 1946 he lived near Souderton, Pennsylvania, later making his home with members of his family in Swarthmore. Always an avid reader, the study of Lincoln and the Civil War period became his hobby.

Dr. Roxby was a member of the Delaware County Medical Society, serving as its president in 1922 while on the staff of the Chester Hospital. He was a Fellow of the American Medical Association and of the College of Physicians of Philadelphia, a member of the Philadelphia Medical Club, the Phi Chi Medical Fraternity, the American Association of University Professors, and the American Association for the Advancement of Science. A charter member of the Swarthmore Methodist Church, he was a former president of its board of trustees. He was also a Mason and member of the Knights of Pythias. During World War I he became an official lecturer for the American Red Cross. From 1926 to 1936 he was president of the Swarthmore Fire and Protective Association.

On August 29, 1900 Dr. Roxby married the former Grace Lydia Coffman who died in 1942. At the time of his death he was survived by four sons, a daughter and eight grandchildren. The eldest son, William, is an engineer; his daughter, Grace, became Mrs. J. David Narbeth. Three of his sons—Harold, Bruce and John—are graduates of the Temple University School of Medicine where their illustrious father had the great happiness and privilege of being one of their teachers.

By nature Dr. Roxby was kind, courteous, tolerant, and always willing to sacrifice his comfort and even his health not only in the interests of students but the welfare of the sick and injured as well. He was an inspiring and excellent teacher, not only because he loved to teach but because of his deep interest in applied anatomy, the importance of which he was well qualified to appreciate because of personal experience in the practice of medicine. While not an investigator he was not lacking in interest in anatomical research. The passing of this splendid physician, anatomist and teacher is regretted not only by his professional colleagues but by his many former students and patients as well. *Requiescat in pace.*

Memoir of Lawrence Curtis (1890–1957)*

By ROBERT H. IVY, M.D.

LAWRENCE CURTIS, A.B., M.D., D.D.S., F.A.C.S., a Fellow of the College of Physicians of Philadelphia since 1937, died on June 8, 1957 at his home, 535 Cornell Avenue, Swarthmore, Pennsylvania, at the age of 67, following a cerebral hemorrhage. He had been an invalid for about four years, forcing his retirement from teaching and practice in 1953.

Doctor Curtis was born February 23, 1890, at Brookfield, Connecticut, where for many years his father was headmaster of the Curtis School for Boys. In 1913 he was graduated from Yale University, where he had been a member of the Track Team and the Glee Club. With the intention of becoming a chemical engineer, upon leaving Yale he enrolled at the Massachusetts Institute of Technology, but decided after two weeks to change to dentistry at the University of Pennsylvania, receiving the D.D.S. degree in 1916. During World War I he served for two years in the U. S. Navy Dental Corps. After the war Dr. Curtis enrolled in the University of Pennsylvania School of Medicine, graduating M.D. in 1923. After internship at the Philadelphia Polyclinic Hospital, he entered the practice of plastic and maxillofacial surgery, in association with the writer. This close association continued for many years, in private and hospital practice and teaching. At the time of his retirement Dr. Curtis was Professor of Plastic Surgery in the Graduate School of Medicine and of Maxillofacial Surgery in the School of Dentistry, and Chief of Plastic Surgery at the Graduate and Presbyterian Hospitals, Philadelphia. Upon retirement, Dr. Curtis was made Professor Emeritus of Maxillofacial Surgery. He was certified by the National Board of Medical Examiners, was a Founder Member of the American Board of Plastic Surgery, a Fellow of the American College of Surgeons, the American Association of Plastic Surgeons, the College of Physicians of Philadelphia, the Philadelphia Academy of Surgery, and a member of the Philadelphia Academy of Stomatology, the American, Pennsylvania State and Philadelphia County Medical and Dental Societies, Sigma Xi, and the Polyologists' Club of Philadelphia. He was a member of the Beta Theta Pi and Nu Sigma Nu Fraternities.

Dr. Curtis made many contributions to the literature, being co-author with R. H. Ivy of "Fractures of the Jaws," which went through three editions. He published numerous papers pertaining to plastic and maxillofacial surgery.

The writer spent many happy years in association with Dr. Curtis. He was a master of his specialty of surgery of the face and jaws; many children with cleft lip, cleft palate and other congenital and acquired deformities have now grown up to lead normal lives in testimony to his skill. He and I were nearly always the first to make morning rounds at the Graduate Hospital, where we were known as "The Dawn Patrol." Dr. Curtis had a very keen sense of humor, which contributed considerably to the success of his teaching and his contact with patients. It is unfortunate that his early, forced retirement prevented him from full enjoyment of the position he eventually attained and which he deserved so well.

Dr. Curtis is survived by his wife, the former Elizabeth Simmons, and three children, Frank Watson Curtis, Richard J. Curtis, and Mrs. John B. Smythe.

* Prepared and published at the request of the Council of the College of Physicians of Philadelphia.

Transactions of the Sections

SECTION ON GENERAL MEDICINE

28 October 1957

The Incidence of Carcinoma in Functioning and Non-Functioning Solitary Thyroid Nodules. William Serber, M.D. (Discusser: Norman G. Schneeberg*, M.D.) (*Abstract* 1, below)

Staphylococcic Septicemia Following Splenectomy in Chronic Leukemia. Abraham M. Frumin*, M.D. (Discusser: Harold Wurzel*, M.D.) (*Abstract* 2, below)

Phenylbutazone as a Presumptive Diagnostic Test of Acute Gout. Philip R. Trommer, M.D. (Discusser: John Lansbury, M.D.) (*Abstract* 3, below)

Prolonged Television Viewing as a Cause of Venous and Arterial Thrombosis in the Legs. Meyer Naide, M.D. (Discusser: Harold L. Israel, M.D.) (*Abstract* 4, below)

25 November 1957

Effects of Insulin and Tolbutamide (Orinase) on Blood Glucose Entry and Removal Rates in Non-Diabetic and Diabetic Patients. A. Gerson Jacobs, M.D., George A. Reichard, M.D., Edward H. Goodman, Jr., M.D., Bernice Friedman, M.D., and Sidney Weinhouse*, Ph.D. (Discusser: Francis D. W. Lukens, M.D.) (*Abstract* 5, below)

Experiences with Pulmonary Actinomycosis in a Tuberculosis Hospital. Maurice E. Goldman*, M.D. (Discusser: David A. Cooper, M.D.) (*Abstract* 6, below)

The Production of Antibody in Patients with Uremia. Irwin L Stoloff*, M.D., Robert Stout*, M.D., Ralph M. Myerson*, M.D., and W. Paul Havens, Jr., M.D. (Discusser: William Bluemle*, M.D.) (*Abstract* 7, below)

Right Hepatic Lobectomy for Carcinoma of the Liver with Three Year Follow-Up. Charles Feinberg*, M.D. (Discusser: Warren Goldburgh*, M.D.) (*Abstract* 8, below)

27 January 1958

Studies on Mitral Stenosis and Insufficiency: Clinical, Physiologic and Pathologic Correlations. Paul Novak*, M.D., Robert Schlant*, M.D., Arthur Phinney*, M.D., and Lewis Dexter*, M.D. (Discusser: Harry Goldberg*, M.D.) (*Abstract* 9, below)

Further Observations on the Use of Myleran in Chronic Myelogenous Leukemia. William Wilson*, M.D. (Discusser: Irving Woldow*, M.D.) (*Abstract* 10, below)

Endocrine Aspects of Lipid Metabolism. Joseph Seifter, M.D., David H. Baeder*, Ph.D., and William J. Beckfield, M.D. (Discusser: William E. Ehrich, M.D.) (*Abstract* 11, below)

Clinical Studies with Lipid Mobilizer Hormone. Chris J. D. Zarafonetis, M.D., Joseph Seifter, M.D., David Baeder*, Ph.D., and John P. Kalas*, M.D. (Discusser: Ralph M. Myerson*, M.D.) (*Abstract* 12, below)

SECTION ON MEDICAL HISTORY

15 October 1957

Meeting sponsored by Temple University School of Medicine. Nicholas Padis, M.D., presiding.

Dr. Frank N. Wilson: A Biographical Sketch[1]. Thomas M. Durant, M.D.

Nicholas Belleville (1753–1831): Aristocratic Physician. Fred B. Rogers, M.D.

Medicine During the Revolutionary War. Fraser Lewis*, A.B.

* By invitation.

[1] Published in *Transactions & Studies*, February, 1958.

19 November 1957

Meeting sponsored by the University of Pennsylvania School of Medicine. Jonathan E. Rhoads, M.D., Provost, presiding.

Historical Remarks on Interrelations of Human and Veterinarian Medicine. Joseph V. Klauder, M.D.

The Role of the Adrenals in the History of Medicine. Charles C. Wolferth, M.D.

William Osler's Medical Treatment at the Hospital of the University of Pennsylvania. Irwin A. Brody*, M.D.

21 January 1958

Meeting sponsored by the Woman's Medical College of Pennsylvania. Dean Marion E. Fay presiding.

The Medical Societies and Women Physicians. Catherine Macfarlane, M.D.

The Evolution of Plastic Surgery. Alma Dea Morani, M.D.

Immunization—Eighteenth versus Twentieth Century. Janet Parker*, A.B., and Elsa Kertesz*, A.B.

SECTION ON OPHTHALMOLOGY[2]

24 October 1957

Recurrent Hemangiopericytoma of the Orbit: Case Report. Edmund B. Spaeth, M.D., and Antonio Valdes-Dapena, M.D.

Ocular Cystinosis: Clinical Report. William C. Frayer, M.D., and Hugo E. Martinez-Roig*, M.D.

The Pathogenesis of the Retinopathy of Prematurity. Francis P. Furgiuele*, M.D.

21 November 1957

Clinical Manifestations of Defective Ocular Wound Healing. John H. Dunnington*, M.D. (Twentieth Annual de Schweinitz Lecture)

[2] Abstracts of the presentations at this Section customarily appear in the *American Journal of Ophthalmology* and the *A.M.A. Archives of Ophthalmology.*

16 January 1958

The Nervous Control of Intraocular Pressure. E. S. Perkins*, F.R.C.S.

SECTION ON OTOLARYNGOLOGY[3]

20 November 1957

Impaired Hearing: Studies of its Physiopathology; Clinical Applications of These Studies. Emanuel Revici*, M.D., and Julian B. Marsh*, M.D.

SECTION ON PUBLIC HEALTH, PREVENTIVE AND INDUSTRIAL MEDICINE

15 October 1957

Influenza: History, Epidemiology and Current Problems[1]. John J. Hanlon, M.D., Tom F. Whayne*, M.D., William P. Boger*, M.D., Klaus Hummeler*, M.D. Werner Henle*, M.D. and Joseph W. Cooch*, M.D.

21 January 1958

Perinatal Mortality and Preventive Aspects of Prematurity. Norman Kendall, M.D., R. Gerald Rice*, M.D. and Elizabeth Kirk Rose, M.D.

ABSTRACTS

Abstract 1

The Incidence of Carcinoma in Functioning and Non-Functioning Solitary Thyroid Nodules. William Serber, M.D., and Harold J. Israel, M.D.

The incidence of carcinoma in multinodular thyroid glands has been reported as varying from 3% to 15%. The solitary nodule is much more suspect, with a reported incidence of carcinoma as high as 34%. With the advent of radioisotopes and scintillation detectors it has become a simple matter to measure the iodine-accumulating function of thyroid nodules by external counting. The question to be

[3] Abstracts of the presentations at this Section customarily appear in the *A.M.A. Archives of Otolaryngology.*

answered is how well does the test predict the presence of carcinoma in the nodule?

We have reviewed the neck scans done in our Isotopes Laboratory during the past 5 years. The group was obviously a selected one, first in the type of patient referred, and second in the ones which were chosen for operation. While the incidence of malignancy in thyroid nodules found there may mean little in the total population, it is certainly relevant to the hospital patient who is already clinically suspect, and with whom we are primarily dealing.

Technique. The patient is given 50 to 100 microcuries of I-131 orally and the neck scanned in 24 hours. Initially a hand scanning technique was used with a grid system of points marked on the neck. During the past 2 years, however, we have employed the more convenient automatic scanner, similar to that described by Bauer *et al.* The presumably normal portion of the gland is usually referred to as *warm*, any area of increased function *hot*, and diminished function *cold*.

Results. In all, 282 scans were done, of which 135 were in patients with solitary thyroid nodules.

73 of the patients with solitary nodules were not operated upon; Of these 5 nodules were hot, 47 warm and 21 cold.

The remaining 62 patients in this group are suitable for study as the result of operation and pathological examination of the nodules. Of these 62 patients, the nodules in 19, or 30%, proved to be carcinoma.

Further analysis disclosed the following:

1. There were 36 patients with hot or warm nodules, 29 warm and 7 hot. Of these, 5 or 14% were carcinoma, 4 warm and 1 hot. The 1 hot nodule which was malignant is, from all other reported series, very unusual. This appeared in a man with a hyperfunctioning thyroid nodule and no areas of activity elsewhere in the neck. He had extensive skeletal metastases, which were also markedly functioning. There were signs of hyperthyroidism, although at operation the normal portion of the thyroid was almost completely degenerated.

2. In the cold nodule group there were 26 patients, with 14 (54%) proving to have carcinoma. This is more than 3 times the incidence in the functioning group.

Comment. The uptake of iodine in abnormal thyroid tissue depends largely upon whether the tissue contains acini and forms colloid. Obviously this happens more frequently in benign than malignant lesions, resulting in a much lower incidence of carcinoma in the functioning nodules. All but one of the malignant functioning nodules were in tumors which at least in some areas were well differentiated and colloid producing. These, incidentally, are the type which can be treated by radioiodine when beyond surgical cure. The remaining nodule was a small papillary carcinoma which was proved to be non-functioning by radioautography, but appeared warm on the preoperative scan, evidently as the result of surrounding and underlying normal tissue. It is possible that this error could be avoided by scanning in several planes with a focusing collimator.

On the other hand, 11 of the cold nodules were benign. Most of these were adenomas with hemorrhage, degeneration and necrosis, and some with cyst formation. Two were fetal or microfollicular adenomas with no colloid formation, and one was a small parathyroid adenoma embedded in the thyroid.

Summary and Conclusions. In a group of 62 patients with solitary thyroid nodules, 30% proved to have carcinoma. Of those which were considered functioning (hot or warm) by a preoperative scan after a tracer dose of radioiodine, 14% were carcinoma, while of the non-functioning nodules (cold) 54% were malignant.

From the data presented it would seem that the solitary cold nodule should certainly be removed. The single warm nodule in this group of patients, though less threatening, appears potentially dangerous. Even the solitary hot nodule, contrary to accepted belief, may prove on rare occasions to be carcinoma.

Abstract 2

STAPHYLOCOCCIC SEPTICEMIA FOLLOWING SPLENECTOMY IN CHRONIC LEUKEMIA. Abraham M. Frumin, M.D.

A 54 year old colored female with a chronic granulocytic leukemia of 3 years duration, treated with x-ray and myleran, developed a refractory anemia despite good control of her leukemic process. A radio-active chromium erthyrocyte survival revealed a half-life of 15 days (normal 28–35 days). There was apparently a selective sequestration of her 'tagged' erythrocytes over the spleen. A splenectomy was done, after which the need for blood transfusions became markedly diminished. Three months later she developed an acute onset of fever, malaise, and mental confusion. A peripheral pancytopenia was found on hospital admission. Blood culture revealed a penicillin resistant staphylococcus albus septicemia. Death occurred within 24 hours. Autopsy revealed bacterial colonies in the kidney and myelofibrosis of the vertebral bone marrow. The relationship of splenectomy to septicemia is presented as regards post-splenectomized children, congenital absence of the spleen, and in laboratory animals. The remote hazards of splenectomy are discussed and the occasional poor prognosis attending the syndrome of hyposplenism is emphasized. The myelofibrotic process here may have been either a stage in the development of leukemia or a manifestation of the previous x-ray therapy.

Abstract 3

PHENYLBUTAZONE AS A PRESUMPTIVE DIAGNOSTIC TEST OF ACUTE GOUT. Philip R. Trommer, M.D.

Phenylbutazone has been used recently in the attack of acute gout. The presumption is made that a case of acute mono-articular arthritis is gout until proven otherwise, or is obviously secondary to a bacterial infection, trauma or another medical condition. Therapy was instituted by 400 to 600 milligrams as the initial dose, followed by 100 milligrams every three hours until relief was obtained. The drug was so administered for no more than 48 and to the most 72 hours. The titratable therapeutic end point was considered to be 48 hours. Permanent relief of the acute attack of pain was considered proof that the diagnosis was gout. Suppression and reoccurrence of symptoms ruled out the diagnosis. Since the number of cases in which this technique has been used is small, a larger number of observations will have to be made to prove that this procedure is a valid therapeutic test. In the cases so treated, the results have been encouraging. The advantages over colchicine alkaloid as a therapeutic test are that the relief is quicker without the toxic side effects of nausea, vomiting and diarrhea.

Abstract 4

PROLONGED TELEVISION VIEWING AS A CAUSE OF VENOUS AND ARTERIAL THROMBOSIS IN THE LEGS. Meyer Naide, M.D.

It has been recognized that stasis is an important factor in the development of venous thrombosis in the legs. The occurrence of thrombosis of major vessels in the legs of four patients who had been watching television for prolonged periods while sitting in awkward positions drew attention to this as a cause for the development of thrombophlebitis and arterial occlusion. Television lends itself peculiarly to prolonged sitting, during which the legs may not be moved much or at all since the viewer must face the screen to watch the program—in contrast to listening to the radio where the listener may move about at will. In two of the patients described, venous thrombosis occurred in the legs-with pulmonary embolism. In the two other patients, thrombosis occurred in a popliteal artery in one, and in a femoral artery in the other. The latter was the result of prolonged sitting in a woman watching television with her legs tucked under her, her favorite way of sitting during television programs.

Television viewers, particularly elderly individuals, should get up and move about every half to one hour, in addition to moving their legs frequently. Girdles and other tight gar-

ments should be removed before prolonged television viewing.

Abstract 5

EFFECTS OF INSULIN AND TOLBUTAMIDE (ORINASE) ON BLOOD GLUCOSE ENTRY AND REMOVAL RATES IN NON-DIABETIC AND DIABETIC PATIENTS. A. Gerson Jacobs, M.D., George A. Reichard, M.D., Edward H. Goodman, Jr., M.D., Bernice Friedman, M.D., and Sidney Weinhouse, Ph.D.

An isotope tracer study, using C^{14}-labeling, (J. Biol. Chem., *225*, 225, 1957) has been applied to a study of the action of 1-butyl-3-p-tolylsulfonylurea (Orinase) in man. Trace doses of glucose, uniformly labeled with C^{14}, are administered to humans with an apparently normal carbohydrate metabolism, and blood samples are withdrawn at frequent intervals. There is a logarithmic drop in the specific activity of the blood glucose, indicative of a "turnover" rate of approximately 1 mg. per 100 ml. per minute. On intravenous injection of insulin (6 to 30 units), the specific activity immediately "plateaus" for 10 to 20 minutes and then resumes its downward trend. It can be calculated that insulin largely inhibits glucose entry into the blood and accelerates its removal 2-fold or more. Essentially similar results were obtained with several diabetic patients who had not received insulin for 48 hours prior to the experiment.

When Orinase was administered intravenously in a dosage of 0.6 to 3 gm., the resultant drop in blood sugar also coincided with "plateauing" of specific activity, indicating an essentially complete suppression of glucose entry into the blood. However, the rate of blood sugar lowering indicated little if any acceleration of removal rate. Orinase action was similar in diabetics who respond to this drug. The results suggest that Orinase exerts its effect primarily on the liver, possibly to inhibit destruction of insulin.

Abstract 6

EXPERIENCES WITH PULMONARY ACTINOMYCOSIS IN A TUBERCULOSIS HOSPITAL. Maurice E. Goldman, M.D.

In the past several years two cases of pulmonary actinomycosis were encountered at the U. S. Public Health Service Hospital, Manhattan Beach, New York.

J. K., a man aged 57, had the onset of bacteriologically proven tuberculosis of the right upper lobe in 1935. After a period of comparative good health, night sweats, cough, weight loss and a diffuse feeling of tightness in his chest began in 1951. The chest x-ray now showed consolidation in the right middle and lower lobes. Although mycobacteria were not demonstrated, he was given a course of streptomycin and PAS without any apparent response. There was, however, some symptomatic improvement after treatment with chloramphenicol.

In 1953 he was readmitted with fever, hemoptysis, and the appearance of being chronically ill. Numerous cultures for tuberculosis and cultures on Sabaroud's medium revealed no growth. He received intermittent courses of penicillin and various broad spectrum antibiotics until his death in 1955 after an acute myocardial infarction.

Sections of the lungs revealed marked fibrosis and infiltration with inflammatory cells. Masses of radiating filaments typical of actinomycosis were seen. No tubercles were noted.

The second patient was a 38 year old white male who had the onset of chills, fever and weight loss in 1954. Chest x-ray demonstrated a right upper lobe infiltration. Penicillin and tetracycline relieved his symptoms but the infiltration persisted. After 12 months of antituberculosis chemotherapy, an apical-posterior resection was performed. No etiological agent had been demonstrated. The specimen revealed fibrosis, multiple small abscesses and "sulfur granules." He was given penicillin post-operatively and his hospital course was uneventful.

Actinomycosis is a chronic granulomatous disease caused by the anaerobic *Actinomyces bovis* and characterized in its full-blown form by multiple abscesses and sinuses in the head and neck, as well as in the abdominal and thoracic organs. "Sulfur granules," if found,

immediately suggest the diagnosis. These are composed of intertwined branch-like mycelia with characteristically radially constructed club-like enlargements.

In the diagnosis of the disease, it is important to make every effort to isolate the fungus. Contrary to popular belief, these anaerobic organisms do not grow like other fungi on Sabaroud's medium. The method of Rosebury, Epps and Clark is useful for examining contaminated specimens. The material is streaked on Bacto brain-heart infusion agar and incubated in Brewer anaerobic jars containing 5% carbon dioxide. Anaerobic actinomyces are not found in nature, but may be recovered from carious teeth, tonsillar crypts, etc.

Pulmonary actinomycosis accounts for about 15% of all cases. Perhaps aspiration of material from the mouth initiates the process. The organism is more likely to obtain a foothold in the presence of pre-existing bronchopulmonary disease, because normal protective mechanisms are absent and the diseased tissue may be relatively anaerobic. Because of the widespread use of potent antibiotics few patients will now present the classical picture of sinuses draining "sulfur granules" and so greater clinical acumen is required.

Abstract 7

THE PRODUCTION OF ANTIBODY IN PATIENTS WITH UREMIA. Irwin L. Stoloff, M.D., Robert Stout, M.D. Ralph M. Myerson, M.D., and W. Paul Havens, Jr., M.D.

The reasons for failure to take by transplants of renal and other tissues are not defined exactly. It has been suggested, however, that the lack of success with this procedure may be related to the production of antibodies to the graft by the recipient. Of interest in this regard was a recent report of nine renal homotransplants into patients with terminal renal failure. Four of these grafts functioned for periods of five weeks to five and one-half months, a duration of viability that was much longer than that seen in experimental animals, and the question was raised whether the state of uremia had reduced the immunologic response of the hosts to the transplants. In an effort to elucidate some information on this point, fourteen patients with azotemia associated with chronic glomerulonephritis, chronic pyelonephritis, and malignant hypertension were studied in regard to their capacity to produce diphtheria antitoxin. Purified diphtheria toxoid was used as antigen, and the anamnestic response in Schick-negative persons was measured, since the production of antitoxin under these circumstances follows a more predictable trend than in the primary response of Schick-positive persons.

With one exception, a regular pattern of response was observed, characterized by a considerable increase in circulating antitoxin by the seventh day after inoculation, reaching a peak usually by the fourteenth or twenty-first day, and thereafter declining gradually. This pattern was qualitatively and quantitatively similar to that found in previous studies of normal persons and of persons with other conditions not known to influence the production of antibody. One patient failed to produce any detectable increase in amount of diphtheria antitoxin, but the remaining thirteen patients had maximum measured amounts of circulating antitoxin ranging from 7.5 to 250 units/ml. serum. Although there was a wide range in amount of azotemia, there was no apparent relationship between its degree of severity and the capacity of the patients to synthesize antibody. Among the most vigorous producers of antitoxin were patients with severest azotemia. The pattern and degree of severity of azotemia varied widely in these patients during the period of immunization and subsequent immunologic response. In certain patients, particularly with obstructive uropathy and chronic pyelonephritis, there was an early sharp reduction in azotemia; in others, the degree of azotemia remained reasonably steady; and in a third group it increased considerably. There was, however, no apparent effect of these highly variable patterns on the trend of immunologic response. These results indicate that azotemia even of severe degree did not suppress the anamnestic response as reflected by the production of circulating antitoxin in these patients.

Abstract 8

RIGHT HEPATIC LOBECTOMY FOR PRIMARY CARCINOMA OF THE LIVER WITH THREE YEAR FOLLOW-UP. Charles Fineberg, M.D.

A case report of a 47 year old white woman with a primary carcinoma confined to the right lobe of the liver was presented. The patient had experienced symptoms of vague epigastric pain dating back to 17 months before admission. At the time of admission she had lost 30 pounds in weight, complained of anorexia, right pleuritic pain, and was experiencing temperature elevation and chills. A moderate anemia was found.

Exploratory laparotomy was performed on December 24, 1954, through a right subcostal incision. A large, smooth mass occupied most of the enlarged right lobe of the liver. Two separate discrete, hard nodules were found projecting from the inferior border of the right lobe of the liver. Frozen-section diagnosis of the lesion was malignant hepatoma. The right pleural cavity was then opened and the lung and diaphragm carefully inspected. No intrathoracic metastases were found. A successful right hepatic lobectomy was performed utilizing the technique of "controlled hepatectomy." The major vessels were ligated outside of the main substance of the liver and the dissection carried out through a relatively avascular intersegmental plane. Injection corrosion casts of the liver will be presented to demonstrate the surgical anatomy of the procedure.

The patient's postoperative period was completely uncomplicated and she was discharged from the hospital on the twenty-first postoperative day. Her liver function studies were always within normal limits in the postoperative period. Graphs of the liver function studies will be shown.

The patient has now been followed for three years; she has regained her preoperative weight and has been able to carry on her usual household duties. Repeat liver function studies reveal no abnormalities. A recurrent mass in the epigastrium was biopsied; histologic sections are inconclusive for diagnosis of metastasis.

Exploratory laparotomy will give the highest percent of correct early diagnosis as well as evidence of resectability in primary carcinoma of the liver. Any patient in whom primary hepatic carcinoma is suspected, who is able to tolerate the procedure, should have early laparotomy if earlier diagnosis and a significant survival rate is to be achieved.

Abstract 9

STUDIES OF MITRAL STENOSIS AND INSUFFICIENCY: SOME CLINICAL AND PHYSIOLOGIC CORRELATIONS. Paul Novak, M.D., Robert Schlant, M.D., Arthur Phinney, M.D., and Lewis Dexter, M.D.

Ten patients with pure mitral stenosis (MS) and 15 patients with predominant mitral insufficiency (MI) were studied clinically and by left heart catheterization. Classification was based upon Korner-Shillingford analysis of indicator dilution curves. Diagnoses were confirmed at operation in 13 cases that came to surgery. Both groups were similar historically and symptomatically. A diastolic murmur was heard in all cases. MS was indicated by the absence of a systolic murmur, the presence of an accentuated 1st sound, pure right ventricular hypertrophy on ECG, the absence of left ventricular enlargement on x-ray, and only slight to moderate left atrial enlargement on x-ray. MI was usually indicated by the presence of a systolic murmur of grade II or greater intensity, a normal mitral 1st sound, left ventricular enlargement and moderate to marked left atrial enlargement on x-ray. The presence or absence of an opening snap was not helpful in this group of patients. The cardiac indices were generally reduced for both groups, averaging 2.1 L/Min/M^2 for the MS patients and 2.8 L/Min/M^2 for the MI patients. Left atrial pressures were similarly elevated for both groups, averaging 26 and 25 mm Hg for the MS and MI cases respectively. Left ventricular diastolic pressures were normal (below 10 mm Hg) in the MS group and elevated in 7 of the MI group. The degree of elevation in the latter group was small however. Mitral diastolic gradients were encoun-

tered in all cases, averaging 22 mm Hg for the MS group and 17 mm Hg for the MI group. These data serve to emphasize that MI is rarely 'pure'. The large gradients and greatly elevated left atrial pressures encountered in the MI group is attributed to the presence of the large diastolic flow across a mildly stenotic valve. Further insight into the patho-physiology of valvular insufficiency depends upon the development of an accurate method to measure regurgitant blood flow.

Abstract 10

FURTHER OBSERVATIONS ON THE USE OF MYLERAN IN CHRONIC MYELOGENOUS LEUKEMIA. William Wilson, M.D.

The use of 'Myleran' (Busulfan) in the control of the clinical features of chronic myeloid leukemia, including peripheral blood and bone marrow abnormalities, has been previously reported. The several clinics publishing these reports have used either intermittent or maintenance programs of therapy. In our studies we have used primarily a maintenance program with an average dose of approximately 3 mgs. per day. From a review of 269 cases, we find that there has been a good response in 230 cases—with failure in only 16. The incidence of cytopenias in this series was approximately 10%. Further observations indicate that the percent of cytopenias induced by Myleran is probably directly proportional to the initial dose of Myleran used in these patients. The patients in our study now total 15; the current status is of particular interest in that 7 of the 15 patients have had an acute myeloblastic relapse which is in keeping with the series reviewed. It would appear from these studies that the patients have not had their life expectancy increased. They certainly have maintained a more normal existence, however, during the course of their disease.

Abstract 11

ENDOCRINE ASPECTS OF LIPID METABOLISM. Joseph Seifter, M.D., David H. Baeder, Ph.D., William J. Beckfield, M.D.

It can readily be demonstrated that a variety of steroids, stresses and diseases cause the release of a clearing factor inhibitor (CFI) in the blood. Under conditions not clearly understood at present CFI can induce hyperlipemia by lipid mobilization (LM). The liver appears to play a critical role in this phenomenon. CFI or LM is released from the posterior pituitary, glucocorticoids being the apparent trigger. The action of LM appears to be limited to mobilization of neutral fat from the mesentery to the liver. There is evidence that LM is not directly involved in the utilization of fat but that another hormone is necessary. When hyperlipemia occurs as a result of LM action the liver contributes the excess cholesterol and phospholipid. Persistent elevation of blood lipids by repeated administration of LM does not cause atheromatosis in rabbits. This does not establish that similar lipemias might not produce arterial disease in humans. Lowering the cholesterol-induced hyperlipemia by hyaluronidase or hyaluronate does not markedly influence the course of atheromatosis in rabbits. This does not establish that lowering of hyperlipemia is of no benefit to humans. The adrenal-pituitary release of LM represents a common mechanism through which a variety of conditions mobilize fat, but is not necessarily the only one since other endocrines are also involved in lipid storage, mobilization and utilization.

Abstract 12

CLINICAL STUDIES WITH LIPID MOBILIZER HORMONE. Chris J. D. Zarafonetis, M.D., Joseph Seifter, M.D., David H. Baeder, Ph.D., and John P. Kalas, M.D.

The lipid mobilizer hormone (LM) of Seifter and Baeder has been under intensive investigation in our clinical and experimental laboratories. Studies include: (1) Determination of the acute response to intravenous injection of LM in fasting patients; (2) Metabolic studies in subjects receiving daily injections of LM over a 2 week period; (3) The effects of prefeeding on the acute response to

LM; and (4) Observations in patients undergoing stress of surgical procedures.

Results may be summarized as follows: 1. As little as 1.2 micrograms of crystalline lipid mobilizer hormone (LM) injected intravenously into fasting subjects elicited a prompt two to three fold rise in plasma fatty acids, cholesterol, and lipid phosphorus. Similar responses were noted with relatively crude plasma dialyzates containing LM when administered in 5 mg. per kilogram amounts.

2. Lipid mobilizer, administered daily for 2 weeks to 4 patients maintained on a diet which provided only 4.8 gm. of fat daily, resulted in a striking elevation of plasma cholesterol, fatty acids and lipid phosphorus, and a definite increase in urinary and fecal cholesterol excretion.

3. These effects were not observed when LM was administered to 2 other subjects who were maintained on diets providing 99 gm. and 153 gm. of fat daily, respectively.

4. The consequences of prefeeding with glucose, cream, or amino acids on the hyperlipemic effect of LM were studied. Meals of glucose or cream, but not of amino acids, were found to block the hyperlipemic effect of intravenously administered LM.

From these and other studies, it appears that triglyceride mobilization occurs following LM administration, but that prefeeding with glucose apparently enables the liver to metabolize the lipids presented to it, thereby preventing peripheral hyperlipemia. Inhibition of the hyperlipemic effect of LM by prefeeding with cream, however, is probably mediated through a different mechanism than that ascribed to the glucose meals.

5. In corollary studies it was found that the stress of surgical procedures uniformly gave rise to triglyceride mobilization from the omental depots; presumably this was secondary to the release of endogenous LM. Peripheral hyperlipemia, however, depended on the manner in which the liver metabolized the lipids presented to it.

These and other observations with LM may hold important implications for certain clinical hyperlipemic states.

List of College Lectures, 1957

2 January 1957

Kern, Richard A. The Use and Abuse of Steroid Therapy in Allergic Disorders. (Hira S. Chouké Lecture I; *Transactions & Studies*, June, 1957)

6 February 1957

Geiling, E. M. K. The Use of the Radioisotopes as an Experimental Tool. (Nathan Lewis Hatfield Lecture XLI; *Transactions & Studies*, August, 1957)

6 March 1957

Bluestone, E. M. Prolonged Illness: The Reorganization of Home and Hospital to Meet the Problem. (James M. Anders Lecture XXXVI; *Transactions & Studies*, June, 1957)

3 April 1957

Papanicolaou, G. N. Diagnostic and Research Aspects of Exfoliative Cytology. (Alvarenga Prize Lecture XVI; *Transactions & Studies*, August, 1957)

8 May 1957

Joint Meeting, Philadelphia County Medical Society and College of Physicians of Philadelphia. Presentation of 34th Annual Strittmatter Award of the Philadelphia County Medical Society to Dr. Stanley P. Reimann by Dr. Truman G. Schnabel, Sr., Chairman of the Award Committee.

2 October 1957

Stadie, William C. Current Views on Insulin Action. (Alvarenga Prize Lecture XVII; *Transactions & Studies*, February, 1958)

6 November 1957

Joint Meeting, College of Physicians of Philadelphia and Philadelphia County Medical Society. Finland, Maxwell. Observations on Antibiotic Resistance of Certain Pathogenic Bacteria. (Mary Scott Newbold Lecture LXXV; *Transactions & Studies*, February, 1958)

11 December 1957

Custer, R. Philip. The So-called Hypersplenic Syndrome: Its Pathogenesis, Recognition and Management. (Thomas Dent Mütter Lecture LXX; *Transactions & Studies*, June, 1958)

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Marie B. Webster
Edward Weiss
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OPHTHALMOLOGY

Francis H. Adler
Leighton F. Appleman
Harold D. Barnshaw
E. Howard Bedrossian
William Braun
Solomon S. Brav
Chapin Carpenter
Burton Chance
Louis B. Cohen
Alfred Cowan
Thomas H. Cowan
George S. Crampton
William J. Creighton
Perce DeLong
Samuel L. DeLong
Edward J. Donnelly
R. T. M. Donnelly
George J. Dublin
I. J. Eisenberg
Van M. Ellis
A. G. Fewell
John K. Finley
H. Walter Forster, Jr.
William C. Frayer
Wilfred E. Fry
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Edward S. Gifford, Jr.
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Alvin Howland
William T. Hunt
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Jay B. Rudolphy
Albert C. Sautter
Harold G. Scheie
James S. Shipman
Edmund B. Spaeth
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Edwin Forbes Tait
Isaac S. Tassman
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Robert H. Trueman
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Superintendent

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January 31, 1958

ELECTED

1952. Abelson, Neva Martin, 32 Woodale Rd.
1926. Adler, Francis Heed, 313 S. 17th St.
1949. Aegerter, Ernest E., 3400 N. Broad St. (40)
1953. Agerty, Horst A., 1111 N. 63rd St. (31)
1936. Alexander, Fay Knight, Germantown Professional Bldg., Greene and Coulter Sts.
1932. Allen, Frederick H., 3915 Henry Ave. (29)
1953. Allman, David B., 104 St. Charles Pl., Atlantic City, N. J.
1935. Alpers, Bernard J., 111 North 49th St.
1930. Appel, Kenneth E., 111 N. 49th St.
1905. Appleman, Leighton Francis, 308 S. 16th St.
1935. Armitage, George L., 400 E. 13th St., Chester, Pa.
1922. Arnett, John H., 2116 Pine St.
1942. Aronson, Joseph D., Henry Phipps Institute, 7th and Lombard Sts.
1952. Ash, Rachel, 255 S. 17th St. (3)
1952. Aston, Melville J., 2507 S. 21st St.
1944. Atkins, Joseph P., 1201 Knox Rd., Wynnewood, Pa.
1956. Atkinson, John B., Chestnut & Copley Rds., Upper Darby, Pa.
1935. Atlee, John L., Jr., 37 E. Orange St., Lancaster, Pa.
1952. Atlee, William A., 37 E. Orange St., Lancaster, Pa.
1958. Ayella, Alfred S., Jr., 1213 S. Broad St. (47)
1935. Bach, Theodore F., 1900 Rittenhouse Sq.
1942. Bachman, Carl, Univ. of Pa. Hospital (4)
1937. Bacon, Emily P., Lankenau Medical Bldg., (31)
1958. Baer, Samuel, 5123 N. Broad St. (41)
1952. Baier, Howard N., 3401 N. Broad St.
1952. Baker, Howard W., 3401 N. Broad St.
1946. Baker, Walter W., 255 S. 17th St.
1958. Ball, Simon, 255 S. 17th St. (3)
1957. Baltzell, William Hewson, 1530 Locust St. (2)
1940. Barba, Philip S., 5919 Greene St.
1943. Barden, Robert P., 8835 Germantown Ave.
1939. Barnshaw, Harold D., 406 Cooper St., Camden, N. J.
1957. Barr, S. Stanley, 255 S. 17th St. (3)
1939. Bartle, Harvey, Jr., 133 S. 36th St.
1932. Batson, Oscar V., 3502 Hamilton St.
1921. Bauer, Edward L., 5501 Greene St. (44)
1933. Bauer, John T., 312 E. Second St., Moorestown, N. J.
1939. Baumann, Frieda, 3300 Henry Ave. (29)
1930. Beardwood, Joseph T., Jr., 2031 Locust St.
1955. Beckfield, William J., Phila. General Hospital, 34th & Curie Ave. (4)
1952. Bedrossian, E. Howard, 2027 Spruce St.
1949. Beecham, Clayton T., 155 W. Walnut Lane (44)
1935. Beerman, Herman 255 S. 17th St. (3)
1942. Behrend, Albert, 255 S. 17th St.
1945. Behrend, Bernard, 5910 Greene St.
1934. Behrend, Moses, 255 S. 17th St.

1949. Beizer, Lawrence H., 304 S. 19th St. (3)
1930. Belk, William Parks, 433 Owen Rd., Wynnewood, Pa.
1936. Bell, Benjamin Tertius, Abington Medical Bldg., Keith & York Rds., Abington, Pa.
1956. Beller, Martin Leonard, 1936 Spruce St. (3)
1947. Bellet, Samuel, 2021 Spruce St.
1954. Bello, Carmen T., 3401 N. Broad St. (40)
1956. Belmont, Owen, 2731 N. 5th St. (33)
1952. Bennett, George A., 1025 Walnut St.
1941. Bernstein, Mitchell, 7609 Mountain Ave. (17)
1951. Bernstine, J. Bernard, 255 S. 17th St.
1956. Berry, Theodore J., 331 E. Lancaster Ave., Wynnewood, Pa.
1957. Biele, Albert M., 1530 Locust St. (2)
1918. Billings, Arthur E., 2020 Spruce St.
1952. Bird, Gustavus C., Jr., 3401 N. Broad St. (40)
1957. Birdsall, Thomas M., 255 S. 17th St. (3)
1949. Bishop, Edward H., 811 Spruce St. (7)
1933. Bishop, Paul A., Pennsylvania Hospital.
1944. Blady, John V., Parkway House, 2201 Benjamin Franklin Pkwy. (30)
1952. Blake, Paul O., 273 N. Lansdowne Ave., Lansdowne, Pa.
1917. Block, Frank B., 305 Tabor Medical Bldg., York & Tabor Rds.
1957. Block, Louis H., 1351 Tabor Rd. (41)
1949. Blumstein, George I., 2039 Delancey St.
1929. Bockus, Henry L., 250 S. 18th St.
1928. Boles, Russell S., Rittenhouse Plaza, 1901 Walnut St.
1923. Bond, Earl D., 111 N. 49th St.
1948. Bookhammer, Robert S., 209 Rittenhouse Claridge (3)
1931. Bortz, Edward Le Roy, 2021 W. Girard Ave.
1921. Borzell, Francis Frank, 4940 Penn St.
1936. Bostwick, Delazon Swift, 106 Linwood Ave., Ardmore, Pa.
1928. Bothe, Frederick A., 255 S. 17th St.
1951. Boucot, Katharine R., 3300 Henry Ave. (29)
1947. Bourland, Henry S., 2219 Garret Rd., Drexel Hill, Pa.
1923. Bower, John O., 2008 Walnut St.
1954. Bowers, Paul A., 2035 Locust St. (3)
1942. Bowie, Morris A., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1907. Bradley, William Nathaniel, Hotel Belgravia, 1811 Chestnut St. (3)
1954. Bralow, S. Philip, 2104 Delancey Pl. (3)
1942. Branen, William, Whitby & Cypress Ave., Yeadon, Pa.
1921. Bransfield, John W., 2101 Spruce St.
1948. Braun, William, 406 Cooper St., Camden, N. J.
1953. Brav, Solomon S., 5575 N. Park Ave. (41)
1953. Breckenridge, Robert L., Our Lady of Lourdes Hosp., 1600 Haddon Ave., Camden 3, N. J.
1946. Briscoe, Clarence Conway, 811 Spruce St. (7)
1953. Brobeck, John R., Univ. of Pa. School of Medicine (4)
1952. Brody, Morris W., 1930 Chestnut St.
1948. Brogan, Edmund J., Thomas Wynne Apartment, Wynnewood, Pa.
1953. Brooke, John A., 1431 Spruce St. (2)
1936. Brown, Clark E., Lankenau Hospital.
1932. Brown, Claude P., 1930 Chestnut St.
1939. Brust, Raymond W., 4710 Chester Ave.
1953. Bucher, Robert M., 3401 N. Broad St. (40)
1952. Bumgardner, Heath D., 3701 N. Broad St. (40)
1940. Burnett, W. Emory, 3401 N. Broad St.

1954. Burros, Harry M., 255 S. 17th St. (3)
1941. Butler, Miriam, Watersmeet, Glen Mills, Pa.
1957. Calhoun, John Alfred, 214 Elm Ave., Swarthmore, Pa.
1928. Campbell, Edward H., 133 S. 36th St.
1952. Campbell, Edward W., 1318 Medical Arts Bldg.
1944. Campion, Richard J., Penllyn Rd., Springhouse, Ambler, Pa.
1931. Cantarow, Abraham, 1025 Walnut St.
1952. Cardone, John B., 831 N. 63rd St.
1935. Carey, Lawrence S., 330 S. 9th St.
1931. Cariss, Walter L., 51 N. 39th St. (4)
1956. Carnwath, John Wallace, Summit & Highland Aves., Jenkintown, Pa.
1930. Carpenter, Chapin, 1930 Chestnut St.
1917. Carson, John B., Newtown Square, Pa.
1956. Carty, James Byron, 51 Hampden Rd., Upper Darby, Pa.
1957. Cattie, Vincent J., 4116 N. Broad St. (40)
1956. Casey, Paul R., Cheltenham & Large Sts. (24)
1937. Castallo, Mario A., 1621 Spruce St.
1943. Castigliano, S. Gordon, 853 Mt. Pleasant Rd., Bryn Mawr, Pa.
1949. Caswell, H. Taylor, 3401 N. Broad St.
1954. Catenacci, Alfred J., 1417 S. Broad St. (47)
1954. Cathcart, Richard T., 739 S. Broad St. (47)
1950. Chamberlain, Richard H., 3400 Spruce St.
1933. Chamberlain, W. Edward, U. S. Veterans Administration, Washington 25, D. C.
1939. Chamberlin, George W., Reading Hospital, Reading, Pa.
1900. Chance, Burton, 1726 Spruce St. (3)
1945. Chance, Burton, Jr., 1726 Spruce St.
1954. Charny, Charles W., 2039 Delancey Pl. (3)
1947. Chouké, Kehar S., P.O. Box 447, Kecoughton, Va.
1945. Cianfrani, Theodore, 1930 Chestnut St.
1939. Ciccone, Emmet F., 2021 Murray St.
1951. Clagett, Augustus H., Jr., 1618 N. Broom St. Wilmington 6, Del.
1929. Clark, Eliot R., 315 S. 41st St.
1934. Clark, Jefferson Hamer, 101 Maple Ave., Wyncote, Pa.
1951. Clark John K., 36th & Spruce Sts. (4)
1947. Clark, Thomas Williams, 9501 Germantown Ave. (18)
1947. Classen, Charles H., Cushman Rd. and Lancaster Ave., Rosemont, Pa.
1958. Closson, Edward W., 2320 S. Broad St. (45)
1910. Cloud, J. Howard, 111 St. Pauls Road, Ardmore, Pa.
1903. Coates, George Morrison, 1721 Pine St.
1957. Cohen, Frank L., 2113 Spruce St. (3)
1941. Cohen, J. Gershon, 255 S. 17th St.
1951. Cohen, Leon Solis-, 1422 Chestnut St.
1949. Cohen, Louis B., 1320 Arrott St.
1907. Cohen, Myer Solis-, 2110 Spruce St.
1953. Cohen, Robert V., 520 Spring Ave., Elkins Park 17, Pa.
1955. Colcher, Abraham E., 269 S. 19th St. (3)
1934. Colgan, Robert C., % Abrams, RD # 1, Bridgeport, Pa.
1934. Collins, Leon Howard, Jr., 133 S. 36th St.
1943. Colonna, Paul C., Univ. of Pa. Hospital.
1949. Conger, Kyril B., 3401 N. Broad St.
1945. Coonel, Pauline, 47 E. Mt. Pleasant Ave.
1930. Cooper, David A., 1520 Spruce St.
1953. Cooper, Donald R., 133 S. 36th St. (4)

1947. Coppolino, John F., 1807 S. Broad St.
1952. Corbit, John D., Jr., 3717 Chestnut St.
1941. Cornelius, Chalmers E., 119 Summit Ave., Jenkintown, Pa.
1911. Cornell, Walter S., Board of Public Education, Parkway and 21st St.
1945. Corrigan, Patrick H., 1720 S. Broad St., Trenton, N. J.
1914. Corson, Edward F., 136 S. 16th St.
1946. Costello, Thomas J., 131 Pennsylvania Avenue, Bryn Mawr, Pa.
1924. Cowan, Alfred, 1930 Chestnut St.
1940. Cowan, Thomas H., 1930 Chestnut St.
1904. Craig, Frank A., 429 Montgomery Ave., Haverford, Pa.
1907. Crampton, George S., 2031 Locust St.
1947. Crane, A. Reynolds, 807 Spruce St.
1937. Crane, Martin P., 2412 N. Broad St.
1920. Creighton, William J., 37 S. 20th St.
1952. Crellin, J. Antrim, 1930 Chestnut St.
1941. Creskoff, Adolph J., 3400 Spruce St.
1955. Crist, Walter A., 211 N. 5th St., Camden, N. J.
1921. Crossan, Edward T., Buttonwood Hall, Conshohocken, Pa.
1937. Crump, Jean, 3300 Henry Ave. (29)
1934. Custer, R. Philip, 126 Grays La., Haverford, Pa.
1938. Dannenberg, Arthur M., 235 S. 15th St.
1951. Daugherty, Earl A., 2025 W. Girard Ave.
1953. Davie, John H., 269 S. 19th St. (3)
1947. Davis, C. Nelson, 133 South 36th St.
1936. Davis, David M., 255 S. 17th St.
1957. Davis, John Evan, Eastern Pa. Psychiatric Institute, Henry Ave. & Abbottsford Rd. (29)
1951. Davis, J. Wallace, 135 S. 18th St.
1937. Davis, Perk Lee, P.O. Box 701, Paoli, Pa.
1935. Deaver, J. Montgomery, Lankenau Medical Bldg., (31)
1957. Decker, John Paul, Pennsylvania Hospital (7)
1957. Dees-Porch, Frances, Glendale & Chestnut St., Upper Darby, Pa.
1947. Dehne, Theodore L., Adams Avenue and Roosevelt Blvd.
1935. Deibert, Irvin Elmer, 538 Cooper St., Camden, N. J.
1923. De Long, Perce, 37 S. 20th St.
1955. De Long, Samuel L., 37 S. 20th St. (3)
1952. DeLuca, Charles Q., 255 S. 17th St.
1952. De Orsay, Ralph H., 1241 Lindale Ave., Drexel Hill, Pa.
1951. De Palma, Anthony F., 248 S. 21st St.
1928. Dewees, A. Lovett, Glen Mills, Del. Co., Pa.
1956. Dietrich, Herbert James, Jr., 2035 Delancey Place (3)
1952. Digilio, Victor A., 2200 St. James Place.
1924. Dillon, Edward S., Conshohocken State Rd., Penn Valley, Narberth, Pa.
1953. Dixon, James P., Dept. of Public Health, City Hall Annex. (7)
1920. Doane, Joseph C., 617 W. Hortter St.
1948. Dohan, Francis Curtis, 80 Princeton Road, Cynwyd, Pa.
1954. Donaldson, James B., 235 N. Broad St. (2)
1946. Donnelly, Andrew J., 33rd and Powelton Ave.
1942. Donnelly, Edward J., 1321 Spruce St.
1933. Donnelly, Jospeh C., 6832 Ogontz Ave.
1937. Donnelly, Robert T. M., 255 S. 17th St.
1954. Downing, Daniel F., 8864 Norwood Ave., (18)
1952. Drayer, Calvin S., 111 N. 49th St.
1949. Dripps, Robert D., 3400 Spruce St.

1935. Duane, William, Jr., 2109 Spruce St. (3)
1956. Dubin, Isadore N., Woman's Medical College (29)
1944. Dublin, George J., 1930 Chestnut St.
1944. Dugger, John H., Episcopal Hospital (25)
1935. Duncan, Garfield G., 330 S. 9th St.
1937. Dunn, Charles W., 265 S. 19th St.
1951. Dunne, Francis S., 133 S. 36th St.
1953. Dupler, Donald A., 4028 Walnut St. (4)
1942. Durant, Thomas M., 3401 N. Broad St.
1947. Durkin, John Keenan, 34 W. Montgomery Ave., Ardmore, Pa.
1942. Dyer, W. Wallace, Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1935. Eads, John T., 607 E. Durham St. (19)
1936. Easby, Mary Hoskins, Woman's Hospital.
1948. Eaton, Francis H., 4007 Chestnut St.
1937. Edeiken, Joseph, 2130 Delancey Pl.
1944. Eger, Sherman A., 2029 Delancey St.
1944. Ehrich, William E., 540 W. Hortter St.
1956. Eiman, John W., Abington Memorial Hospital, Abington, Pa.
1953. Eisenberg, Isadore J., 1520 N. 2d St., Harrisburg, Pa.
1946. Elfman, Louis Kenneth, 6330 Lebanon Avenue.
1949. Elkinton, J. Russell, Oak Lane, Moylan, Pa.
1957. Ellis, Richard A., 269 S. 19th St. (3)
1955. Ellis, Samuel, 541 S. 46th St., (43)
1939. Ellis, Van Mashburn, 1528 Spruce St. (2)
1928. Ellison, Richard T., 8601 Stenton Ave.
1936. Ellson, J. Vernon, 807 Spruce St.
1904. Elmer, Walter G., 1801 Pine St.
1937. Elsom, Kendall A., Maloney Clinic Bldg., 36th & Spruce St. (4)
1934. Ely, William C., 3912 Chestnut St.
1932. Engel, Gilson C., Lankenau Medical Bldg. (31)
1945. English, O. Spurgeon, 3401 N. Broad St. (40)
1942. Erb, William H., 133 S. 36th St.
1957. Erdman II, William James, 3400 Spruce St. (4)
1950. Ersner, Matthew S., 1915 Spruce St.
1957. Etzel, Michael M., 9025 Frankford Ave. (14)
1954. Evans, Harry D., Jr., 250 S. 18th St. (3)
1954. Evans, William W., Box 2, Bryn Mawr, Pa.
1948. Everts, Glenn S., 5515 Wissahickon Ave., Apt. D-403.
1955. Eynon, Harold K., 538 Cooper St., Camden, N. J.
1946. Farell, David M., 1912 Spruce St.
1903. Farr, Clifford B., Bryn Mawr, Pa.
1945. Farrar, George Elbert, Jr., 528 Scott Rd., Gladwyne, Pa.
1953. Farrell, Harry L., 1930 Chestnut St. (3)
1930. Farrell, John T., Jr., 255 S. 17th St.
1935. Ferguson, Lewis Kraeer, 133 S. 36th St.
1936. Fetter, Ferdinand, 322 S. 21st St.
1945. Fetter, John S., 842 Worrell Rd., Jenkintown, Pa.
1935. Fetter, Theodore R., 255 S. 17th St.
1924. Fewell, Alexander G., 1924 Pine St.
1952. Fields, Harry, 133 S. 36th St.
1955. Finestone, Albert J., 2039 Pine St. (3)
1943. Finkelstein, Arthur, 480 Latch's Lane, Merion, Pa.
1955. Finkelstein, David, 1930 Chestnut St. (3)

1955. Finley, John K., 527 Welsh St., Chester, Pa.
1954. Finn, Joseph L., 7109 Rising Sun Ave. (11)
1947. First, Arthur, 1714 Spruce St.
1954. Fischer, Carl C., Germantown Professional Bldg. (44)
1945. Fiske, Frederick A., 1530 Locust St.
1956. Fite, Franklin K., Germantown Hospital (44)
1952. Fitts, William T., Jr., 3400 Spruce St.
1928. Fitz-Hugh, Thomas, Jr., 2016 Delancey Pl.
1952. Flexner, Louis B., Univ. of Pa. School of Medicine (4)
1928. Flick, John B., 819 Black Rock Rd., Gladwyne, Pa.
1954. Flick, John B., Jr., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1952. Flinn, Lewis B., 503 Delaware Ave., Wilmington, Del.
1939. Flippin, Harrison F., Lankenau Hospital, (30)
1951. Ford, Elbert S. C., 255 S. 17th St.
1957. Forman, Simon B., 255 S. 17th St. (3)
1957. Fornwalt, George R., Glendale & Chestnut Sts., Upper Darby, Pa.
1954. Forster, H. Walter, Jr., 37 S. 20th St. (3)
1941. Fox, C. Calvin, 1806 Spruce St.
1906. Fraley, Frederick, 6005 Overbrook Ave. (31)
1957. Frankel, Donald S., 255 S. 17th St. (3)
1955. Frayer, William C., 313 S. 17th St. (3)
1941. Frazier, William Doane, 419 Gilpin Rd., Narberth, Pa.
1952. Freed, Herbert, 255 S. 17th St.
1956. Freeman, Joseph T., 8-A Rittenhouse Plaza (3)
1953. Fried, Paul H., 1812 Spruce St. (3)
1955. Friedenberg, Zachary B., 133 S. 36th St. (4)
1951. Friedman, Paul Sigmund, 1422 Chestnut St.
1958. Freiwald, Milton J., 1530 Spruce St. (2)
1933. Fritch, James Scott, 269 S. 19th St.
1937. Fritz, Herbert H., Pennswood Rd., Bryn Mawr, Pa.
1953. Fruchter, Joseph M., 601 W. Cliveden St., C-221 (19)
1940. Fry, Kenneth E., 1719 Rittenhouse Sq.
1935. Fry, Wilfred Eyles, 1930 Chestnut St.
1937. Furlong, Thomas F., Jr., Times Medical Building, Ardmore, Pa.
1954. Gambescia, Joseph M., 255 S. 17th St. (3)
1935. Gammon, Geo. D., Univ. of Pa. Hospital (4)
1951. Garlichs, Richard W., 216 N. Manoa Road, Havertown, Pa.
1931. Garner, Vaughn C., Germantown Professional Building
1953. Garnet, James D., 807 Spruce St. (7)
1950. Garvin, Eugene J., 533 S. 46th St. (43)
1953. Geckeler, Edwin O., 269 S. 19th St. (3)
1952. Gefter, William I., 366 Penn Rd., Wynnewood, Pa.
1935. Geist, Donald C., 1930 Chestnut St.
1955. Gelfand, David, 1722 Pine St., (3)
1954. German, George B., 429 Cooper St., Camden, N. J.
1955. Gettes, Bernard C., 128 Overhill Rd., Cynwyd, Pa.
1934. Gibbon, John H., Jr., 1025 Walnut St.
1939. Gibson, Glen Gregory, 2031 Locust St.
1944. Gifford, Edward S., Jr., 1913 Spruce St.
1954. Gilbert, Philip D., Cooper Hospital, Camden, N. J.
1954. Giletto, Basil J., 2020 Locust St. (3)
1920. Gill, A. Bruce, 1603 Normandy Drive, Mt. Dora, Fla.
1956. Gill, Robert J., 801 Spruce St. (7)

1927. Gilmour, William R., 6616 Woodland Ave. (42)
1952. Gilpin, Sherman F., 3701 N. Broad St.
1949. Ginsburg, Isadore W., 3401 N. Broad St. (40)
1931. Giordano, Anthony A. S., 1819 S. Broad St.
1954. Gislason, Gerhard J., Medical Arts Bldg. (2)
1954. Glover, Robert P., 269 S. 19th St. (3)
1953. Godfrey, Lincoln, 255 S. 17th St. (3)
1956. Goldberg, Harry, 249 N. Broad St. (2)
1945. Goldberg, Samuel J., 1723 Pine St.
1933. Goldburgh, Harold L., 1932 Spruce St.
1935. Goldsmith, N. Ralph, 1351 Tabor Rd.
1949. Gopadze, Illarion I., 1809 Delancey Pl.
1956. Goracci, Armando F., 2040 Poplar St. (30)
1937. Gordon, William, 5345 Spruce St.
1956. Gouley, Benjamin, 5577 N. Park Ave. (41)
1941. Gouterman, Joseph I., 1930 Chestnut St.
1957. Grahn, Henry Victor, 5132 Chester Ave. (43)
1926. Grant, Francis Clark, 750 Germantown Pike, Lafayette Hill, Pa.
1958. Greco, Toby A., 2506 S. 20th St. (45)
1940. Greene, Lloyd B., 136 S. 16th St.
1952. Greening, Roy R., 3400 Spruce St.
1955. Greenstein, Raphael H., 1710 Pine St. (3)
1934. Griffith, John Q., Jr., 6 N. Fredericksburg Ave., Margate, N. J.
1945. Griffiths, John E., Mermont Apartments, Bryn Mawr, Pa.
1941. Groff, Robert A., Univ. of Pa. Hospital. (4)
1952. Grotzinger, Paul J., 2121 Valley Road, Huntingdon Valley, Pa.
1952. Grove, D. Dwight, 230 N. Broad St.
1945. György, Paul, Univ. of Pa. School of Medicine (4)
1935. Hadden, Samuel B., 250 S. 18th St. (3)
1951. Hafkenschiel, Joseph H., 3600 Spruce St.
1945. Hahn, George A., 255 S. 17th St.
1935. Haines, Harlan F., 134 S. State Rd., Upper Darby, Pa.
1955. Hallahan, John D., 104 W. Front St., Media, Pa.
1951. Hallett, Joseph W., 1001 Medical Arts Bldg., 16 & Walnut Sts.
1939. Hamblock, Leonard C., 1632 Spruce St.
1954. Hand, B. Marvin, 269 S. 19th St. (3)
1938. Hand, John G., 1724 Pine St.
1947. Hanes, William James, 218 E. Beechtree Lane, Wayne, Pa.
1950. Hansen, A. Victor, 3401 N. Broad St. (40)
1957. Harasym, Emil L., 952 N. Franklin St. (23)
1956. Harbert, Frederick, Jefferson Hospital (7)
1952. Harer, W. Benson, State Rd. & Rogers Ave., Bywood, Pa.
1951. Harkins, Herbert P., 1930 Chestnut St.
1932. Harris, Stanley E., 229 Maple Ave., Delanco, N. J.
1948. Harris, T. N., 2222 N. 53rd St.
1929. Harrison, Francis G., 1900 Spruce St.
1926. Hartmann, Fred L., 1914 Pine St.
1946. Harvey, Edith E., 406 York Rd., Jenkintown, Pa.
1947. Harvey, Rolfe Marsh, 669 Mill Rd., Villanova, Pa.
1935. Haskell, Benjamin F., 1427 Spruce St.
1946. Hatfield, C. Alexander, 330 S. 9th St.
1947. Havens, Walter Paul, Jr., 300 Cherry Lane, Wynnewood, Pa.
1947. Hawthorne, Herbert Reid, 255 S. 17th St. (3)

1952. Hayllar, Benjamin L., 801 Medical Arts Bldg.
1957. Hedges, Thomas R., Jr., 1930 Chestnut St. (3)
1946. Hendrickson, Frank O., 140 N. Rolling Rd., Springfield, Pa.
1953. Henry, George C., 3400 N. Broad St. (40)
1944. Herbut, Peter A., Jefferson Medical College Hospital
1953. *Herrick, William C., 4632 Denwood St., La Mesa, California
1951. Herrman, Clinton S., 1301 Spruce St., (7)
1954. Herron, James R., 1486 Haddon Ave., Camden 3, N. J.
1957. Hess, Catherine B., 4 W. Mt. Pleasant Ave., (19)
1924. Hewson, William, 1614 Locust St.
1949. Heyl, W. Meredith, 100 W. Coulter St.
1956. Hildreth, Eugene A., University of Penna. Hospital (4)
1952. Hinkson, DeHaven, 329 N. 40th St.
1924. Hirst, John C., 2d., 500 N. 20th St.
1943. Hitschler, William J., Bethlehem Pike & Summit (18)
1944. Hneleski, Ignatius S., 802 S. 48th St.
1943. Hockaday, Agnes, 316 Shadeland Ave., Drexel Hill, Pa.
1939. Hodes, Philip J., Univ. of Pa. Hospital (4)
1947. Hodges, John H., 1025 Walnut St.
1954. Hoeffel, Joseph M., Jr., 330 S. 9th St. (7)
1948. Hoffman, George L., Jr., 133 S. 36th St.
1954. Hollander, George, 3500 Vista St. (36)
1949. Hollander, Joseph L., 36th & Spruce Sts. (4)
1932. Hollingsworth, I. Pemberton, 411 N. Walnut St., West Chester, Pa.
1951. Hollis, Charles B., 1930 Chestnut St.
1952. Holloway, Edward E., 1739 W. Montgomery Ave.
1949. Hopkins, Henry U., Garden Court Apts., 47th & Pine Sts.
1953. Horan, Charles A., 734 N. 63rd St. (31)
1946. Horan, Gerald W., 5819 Chester Ave.
1947. Horwitz, Orville, Hospital of University of Pa. (4)
1950. Houlihan, Carl T., 728 S. 60th St.
1944. Housel, Edmund L., 255 S. 17th St.
1928. Houser, Karl Musser, 2035 Delancey Pl.
1948. Howland, Alvin Wilcox, 255 S. 17th St.
1946. Howlson, John Yeatts, 316 Lancaster Ave., Wayne, Pa.
1951. Hubbard, John P., University of Penna. School of Medicine.
1947. Huber, John Franklin, Temple University School of Medicine. (40)
1937. Hughes, Joseph, 111 N. 49th St.
1939. Hughes, P. Boland, 419 Hillbrook Rd., Bryn Mawr., Pa.
1951. Hundley, J. Warren, 3818 Chestnut St.
1954. Hunsicker, William C., Jr., 255 S. 17th St. (3)
1946. Hunt, William T., Jr., 1930 Chestnut St.
1921. Hunter, Robert John, 928 N. 63rd St. (31)
1952. Hyman, Harold L., 3401 N. Broad St. (40)
1950. Imbriglia, Joseph E., 329 Shadeland Ave., Drexel Hill, Pa.
1952. Imperiale, C. Charles, 1331 Pine St.
1935. Ingelby, Helen, Jewish Hospital, York & Tabor Rds.
1949. Ingraham, Norman R., Jr., Stenton and Whitemarsh Ave.
1957. Isaacson, Howard, Haverford Ave. & Drexel Rd.
1951. Isard, Harold J., Mt. Sinai Hospital, 5th & Reed sts.
1951. Israel, Harold L., 304 S. 19th St. (3)

* Military service.

1947. Israel, S. Leon, 2116 Spruce St.
1952. Iverson, Preston C., 1930 Chestnut St.
1917. Jackson, Chevalier, 3401 N. Broad St.
1932. Jackson, Chevalier L., 3401 N. Broad St.
1934. Jacobs, Maurice, 1831 Delancey Place.
1947. Jaeger, Rudolph, Jefferson Medical College Hospital.
1952. Janton, O. Henry, 2008 Walnut St. (3)
1941. Jeffers, William A., University of Pa. Hospital. (4)
1955. Jernstrom, Paul H., Jefferson Hospital. (7)
1942. Johnson, Julian, 406 Conshohocken State Rd., Narberth, Pa.
1938. Johnson, Thomas A., 135 S. 18th St. (3)
1952. Jonas, Karl C., 2601 Parkway.
1918. Jonas, Leon, 255 S. 17th St.
1924. Jones, Harold W., 1930 Chestnut St.
1957. Jordan, Luke W., 255 S. 17th St. (3)
1957. Kacher, Leon, 2037 Pine St. (3)
1936. Kain, Thomas M., 403 Cooper St., Camden, N. J.
1957. Kane, Sydney H., 3458 Cottman Ave. (49)
1948. Kaplan, Louis, 2040 Pine St.
1938. Kasper, Kelvin A., 135 S. 18th St.
1945. Katz, G. Henry, 111 N. 49th St.
1941. Kauffman, M. Luther, Medical Arts Bldg., Jenkintown, Pa.
1947. Kay, Calvin Frederick, Univ. of Pa. Hosptial. (4)
1954. Kaye, Robert, Children's Hospital, 1740 Bainbridge St. (46)
1954. Kaye, Robert, Children's Hospital, 1740 Bainbridge St. (46)
1947. Keefer, George Pfahler, 3708 Woodland Ave., Drexel Hill, Pa.
1949. Keiserman, Joseph, 5460 Baltimore Ave.
1935. Kelly, George F. J., N.E. Cor. 20th and Chestnut Sts.
1932. Kelly, Herbert T., 1900 Spruce St.
1912. Kelly, Thomas C., 105 School Lane.
1941. Kennedy, Patrick J., 32 Hampden Rd., Upper Darby, Pa.
1947. Kennedy, William Blair, Univ. of Pa. School of Medicine. (4)
1948. Kern, Franklin Moore, 903 Nicholson Rd., Wynnewood, Pa.
1921. Kern, Richard A., Temple University Hospital. (40)
1935. Keyes, Baldwin L., 2031 Locust St.
1930. Kimbrough, Robert A., Jr., 807 Spruce St.
1936. King, Orville C., 330 S. 9th St.
1952. Kirshner, Jacob J., 1930 Chestnut St.
1920. Klauder, Joseph V., 1934 Spruce St.
1920. Klein, Thomas, 250 S. 18th St.
1952. Kleinbart, Morris, 1922 Pine St.
1954. Kligman, Albert M., 36th & Spruce Sts. (4)
1934. Kline, Oram R., 514 Cooper St., Camden, N. J.
1948. Klingensmith, Paul O., 133 S. 36th St.
1956. Klinghoffer, June F., 5501 Green St. (44)
1932. Klopp, John W., Gwynedd Valley, Pa.
1919. Knipe, Norman L., 514 Baird Rd., Merion, Pa.
1945. Kobler, H. B., 658 N. 63rd St.
1914. Kolmer, John A., Cynwyd, Pa.
1957. Koltes, John A., Jefferson Hospital, 14th Annex, 10th & Sansom St. (7)
1936. Konzelmann, Frank Williamson, 12 E. Lenox St., Chevy Chase, Md.
1949. Koop, C. Everett, 1740 Bainbridge St.
1952. Kornblueh, Igho H., Welsh Rd., & Verree Rd. (15)

1941. Krall, J. Thomas, 1927 Spruce St.
1948. Kramer, David W., 2007 Pine St.
1954. Krasnoff, Sidney O., Tabor Medical Bldg. (41)
1944. Krauss, Frederick Harold, 16th & Walnut Sts.
1952. Kravitz, Charles H., 1726 Widener Pl.
1949. Kremer, David N., 1918 Pine St.
1949. Kressler, Robert J., 330 S. 9th St.
1941. Krewson, William E., 3rd. 1930 Chestnut St.
1914. Krumbhaar, Edward B., Univ. of Pa. School of Medicine (4)
1953. Krumperman, LeRoy W., 3401 N. Broad St. (40)
1947. Kuhlenbeck, Hartwig, Woman's Medical College.
1947. La Boccetta, Alfred Charles, 2nd and Luzerne Sts.
1952. Lachman, John W., 3401 N. Broad St. (40)
1949. La Clair, Charles H., Jr., 1021 W. Main Wt., Norristown, Pa.
1952. Lafferty, Henry D., 37 S. 20th St.
1951. Lame, Edwin L., 51 N. 39th St.
1050. Lamont, Austin, 3400 Spruce St. (4)
1946. Lampe, William T., 4207 Tyson Ave.
1952. Lang, Warren R., 1012 Walnut St. (7)
1941. Langner, Paul H., Jr., 1208 Edmonds Ave., Drexel Hill, Pa.
1945. Lansbury, John, 3401 N. Broad St. (40)
1926. Laws, George M., 1907 Spruce St.
1936. Leaman, William G., Jr., Presidential Apts: Adams House B-909.
1950. Learner, Norman, 3701 N. Broad St. (40)
1920. Leavitt, Frederic Headley, 1527 Pine St.
1957. Lee, Charles Trumbull Lee, Jr., 15 E. Highland Ave. (18)
1941. Leberman, Paul R., 136 S. 16th St.
1942. Lehman, James A., 255 S. 17th St.
1952. Lehman, J. Stauffer, 230 N. Broad St.
1951. Leivy, Frank E., 1321 Spruce St.
1944. Lell, William A., 333 S. 18th St. (3)
1935. Lemmon, William T., 133 S. 36th St.
1943. Leopold, Irving H., 1930 Chestnut St.
1955. Leopold, Robert L., 269 S. 19th St. (3)
1944. Lettiere, Anthony J., 425 E. State St., Trenton, N. J.
1933. Levering, J. Walter, Abington Memorial Hospital, Abington, Pa.
1958. Levine, Samuel, 7100 N. 19th St. (38)
1958. LeWinn, Edward B., 1351 Devereaux Ave. (11)
1915. Lewis, Fielding O., Providence Road, Media, Pa.
1938. Lewis, James P., 3815 Chestnut St.
1955. Lieberman, George E., 2019 Pine St. (3)
1948. Lieberman, Louis M., 923 Belmont Ave.
1956. Likoff, William, 249 N. Broad St. (2)
1940. Limberger, William A., 301 S. Church St., West Chester, Pa.
1958. Lin, David Y. P., 2228 S. Broad St. (45)
1938. Lindauer, M. August, 133 S. 36th St.
1956. Lindquist, John N., 422 Sabine Ave., Wynnewood, Pa.
1927. Lindsey, Walter H., 810 W. Dauphin St.
1936. Lintgen, Charles, 1930 Chestnut St.
1958. Lipschutz, Arthur, 7974 Fayette St. (19)
1953. Lipsius, Edward I., 319 S. 16th St. (3)
1945. Lisker, Samuel, 255 S. 17th St. (3)
1944. Livezey, Mary M., 7200 Cresheim Rd.

1936. Llewellyn, Thomas H., 910 N. 63rd St.
1907. Lodholz, Edward, The Fairfax, 43rd & Locust Sts.
1931. Loewenberg, Samuel A., 1905 Spruce St.
1951. Long, Joseph P., 1930 Chestnut St.
1935. Long, William L., 2025 Walnut St.
1931. Longaker, Edwin P., 41 E. Montgomery Ave., Ardmore, Pa.
1951. Lorber, Stanley H., 3701 N. Broad St. (40)
1936. Lucchesi, Pascal Francis, 601 E. Gorgas Lane.
1932. Lukens, Francis D. W., Univ. of Pa. Hospital (4)
1939. Luongo, Romeo A., 2054 Locust St.
1947. Lurie, Max B., Henry Phipps Institute, 7th and Lombard Sts.
1951. Luscombe, Herbert A., 136 S. 16th St.
1952. Lutman, Frank C., 100 W. Coulter St.
1919. Lynch, Frank B., Jr., Veterans Administration Hospital, Coatesville, Pa.
1950. Lynch, J. Edward, 255 S. 17th St.
1953. Lyons, John W., 255 S. 17th St. (3)
1933. McAndrews, Leo F., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1952. McCabe, Edward S., 136 S. 16th St. (2)
1932. McCahey, James F., 1534 Pine St.
1900. McCarthy, Daniel J., 2025 Walnut St.
1936. McCarthy, Patrick A., 229 E. Price St. (44)
1935. McClenahan, William U., 1 Summit Ave.
1953. McCloskey, Joseph F., Jefferson Hospital. (7)
1955. McClure, Carroll R., 17 S. Church St., W. Chester, Pa.
1957. McConnell, Edward L., Jr., 2230 S. Broad St. (45)
1935. McConnell, James W., 7719 Parkview Rd., Upper Darby, Pa.
1934. McCouch, Grayson P., Univ. of Pa. School of Medicine (4)
1938. McCrea, Lowrain E., 1930 Chestnut St.
1954. McCrory, Wallace W., Children's Hospital, 1740 Bainbridge St. (46)
1937. McCutcheon, Morton, Cambridge Apts.
1942. McDonald, P. Robb, 1930 Chestnut St.
1953. McDonnell, William V., 1025 Walnut St. (7)
1952. McElroy, Robert C., 133 S. 36th St.
1950. McFadden, William M., 1187 E. Washington Lane
1949. McGavic, John S., 601 Montgomery Ave., Bryn Mawr, Pa.
1945. McGee, Lemuel Clyde, Hercules Powder Company, Wilmington, Del.
1954. McGehee, Edward H., 15 E. Highland Ave. (18)
1952. McGlade, Thomas H., 719 Cooper St., Camden, N. J.
1956. McGrath, Raymond J., 1720 Spruce St. (3)
1933. McLaughlin, James S., 330 S. 9th St.
1924. McMillan, Thomas M., 1901 Walnut St. (3)
1924. McPhedran, F. Maurice, Germantown Hosp., Penn and Chew Sts.
1955. McStravog, Lawrence J., 6910 Market St., Upper Darby, Pa.
1954. MacFadyen, Bruce V., 135 S. 18th St. (3)
1943. Macfarlan, Douglas, 1805 Chestnut St.
1932. Macfarlane, Catharine, 136 S. 16th St.
1947. Machella, Thomas E., Univ. of Pa. Hospital. (4)
1950. Mackmull, Gulden, Greene & Coulter St. (44)
1949. MacNeal, Perry Scott, 330 S. 9th St.
1939. Macneill, Norman N., 5807 Chew St.
1951. Mac Neish, W. J., Medical Arts Bldg., 16th & Walnut Sts.
1955. Macy, Dorothy, Jr., 3 Beechwood Rd., Pine Ridge, Media, R.D. 3, Pa.
1957. Madow, Leo, 111 N. 49th St. (39)

1935. Maeder, LeRoy M. A., 1910 Rittenhouse Sq.
1952. Mahoney, J. Francis, 250 S. 18th St.
1942. Manges, Lewis C., Jr., 2001 Delancey Place (3)
1954. Manges, Willis E., Methodist Hospital, Broad & Wolf Sts. (48)
1936. Mann, Bernard, 2019 Pine St.
1956. Manstein, George, 1351 Tabor Rd. (41)
1953. Marbach, A. Herbert, 1307 Tabor Rd. (41)
1948. Marden, Philip Ayer, 1910 Spruce St. (3)
1937. Margolies, Alexander, 1351 Tabor Rd.
1950. Mark, George E., 3401 N. Broad St. (40)
1950. Marshall, E. Wayne, Jr., 1520 Spruce St.
1951. Martin, William L., Hahnemann Hospital.
1952. Martucci, Albert A., 1460 E. Cheltenham Ave.
1953. Marx, Halvey E., 282 N. Lansdowne Ave., Lansdowne, Pa.
1953. Massey, Franklin C., 136 S. 16th St. (2)
1935. Matthews, Robert A., 1025 Walnut St. (7)
1939. May, Hans, 255 S. 17th St.
1958. Mays, Ralph Whiteman, 154 W. Tulpehocken St. (44)
1951. Mayock, Robert L., 3600 Spruce St. (4)
1952. Mecray, Paul, Jr., 405 Loucroft Ave., Haddonfield, N. J.
1951. Medinger, Frederick G., 255 S. 17th St.
1955. Melnick, Theodore, 1152 N. 63rd St. (31)
1941. Mendell, Theodore H., 2023 Spruce St.
1951. Mendelssohn, Edwin, 255 S. 17th St.
1949. Menkin, Valy, 3401 N. Broad St.
1943. Meranze, David R., 1031 Lakeside Ave.
1956. Merves, Louis, 1930 Chestnut St. (3)
1955. Mervine, Thomas B., 133 S. 36th St. (4)
1955. Meyer, Eugene A., 1438 Mt. Ephraim Ave., Camden, N. J
1937. Meyer, George Phillip, 410 Haddon Ave., Camden, N. J.
1956. Miller, Bernard Joseph, 340 S. 15th St. (3)
1935. Miller, Ford A., 4016 Chestnut St.
1946. Miller, Franklin R., Snyder-Jones Clinic, Winfield, Kan.
1939. Miller, Malcolm W., Lankenau Medical Bldg. (31)
1939. Miller, Merle M., 6013 Greene St.
1932. Miller, M. Valentine, 114 W. Phil-Ellena St.
1921. Miller, T. Grier, 133 S. 36th St.
1955. Miller, William H., Fitzgerald Mercy Hospital, Darby, Pa.
1952. Minehart, John R., 4821 Germantown Ave.
1952. Mintz, S. S., 1930 Chestnut St., (3)
1937. Missett, Joseph Vincent, Jr., 2031 Locust St.
1904. Mitchell, Charles Franklin, 2003 Pine St.
1950. Mitchell, John McK., Univ. of Pa. School of Medicine. (4)
1952. Mitchell, Robert McNair, 330 S. 9th St.
1932. Mohler, Roy W., 1806 Spruce St.
1936. Montgomery, Hugh, 119 Glenn Road, Ardmore, Pa.
1936. Montgomery, John B., 1930 Chestnut St.
1932. Montgomery, Thaddeus L., 2031 Locust St.
1935. Moore, John Royal, 3401 N. Broad St.
1958. Moore, Samuel R., 4601 Market St. (39)
1947. Moore, Matthew Thibaud, 1813 Delancey Pl.
1924. Moorhead, Stirling W., 1523 Pine St.
1936. Morgan, David R., Jefferson Medical College.

1893. Morris, Elliston J., 439 Midland Ave., St. Davids, Del. Co., Pa.
1944. Morris, Harold H., Villa Nova, Pa.
1945. Morris, I. Paul, 1939 Cheltenham Ave.
1957. Moyer, David G., 701 W. Main St., Lansdale, Pa.
1941. Mucklé, Craig Wright, 330 S. 9th St. (7)
1929. Mudd, Stuart, Department of Bacteriology, Univ. of Pa. School of Medicine.
1949. Mulholland, Stanford W., 22nd & Parkway.
1935. Mullen, Carroll Richard, 2025 Locust St.
1934. Mullen, Edward A., 472 Roxborough Ave.
1930. Murphy, Douglas P., Univ. if Pa. Hospital. (4)
1953. Murphy, Edward J., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1955. Murtagh, Frederick, 3701 N. Broad St. (40)
1955. Mussells, F. Lloyd, Philadelphia General Hospital (4)
1951. Myers, David, 3701 N. Broad St. (40)
1955. Nachod, Grace R., 5501 Greene St. (44)
1945. Naide, Meyer, 2034 Spruce St.
1951. Naidoff, David, 3500 Tudor St. (36)
1950. Nardone, Anthony A., 912 S. 49th St.
1948. Neese, Paul H., 17 Derwen Road, Cynwyd, Pa.
1936. Nelson, Guy M., 255 S. 17th St.
1943. Nelson, Waldo E., 615 Moreno Rd., Narberth, Pa.
1955. Nemir, Paul, Jr., 255 S. 17th St. (3)
1905. Newcomet, William S., 3501 Baring St.
1938. Newton, Zachariah B., 601 E. Sedgwick St.
1957. Nichols, Russell Lloyd, Jefferson Medical College Hospital, (7)
1935. Nicholson, Jesse Thompson, 1740 Bainbridge St. (46)
1947. Noone, Ernest L., 4501 Cedar Lane, Drexel Hill, Pa.
1905. Norris, Charles C., Darby and Goshen Roads, Bryn Mawr, Pa.
1954. Norris, Charles M., 3401 N. Broad St. (40)
1905. Norris, George W., 250 S. 18th St. (3)
1938. Norris, Robert F., 513 Wynnewood Ave., Wynnewood, Pa.
1957. Oakey, Richard S., Jr., 309 Medical Bldg., Lankenau Hospital (30)
1947. O'Keefe, John J., 255 South 17th St.
1954. Olsen, Axel K., 230 N. Broad St. (2)
1913. O'Neal, Alexander Hay, St. Davids, Pa.
1949. O'Neill, James F., 140 Roslyn Ave., Glenside, Pa.
1954. O'Neill, Thomas J. E., 269 S. 19th St. (3)
1947. Ornsteen, A. M., 2007 Delancey Pl.
1947. Ornston, Darius Gray, 36 Carpenter Lane.
1936. Orr, Theodore E., 1930 Chestnut St.
1955. Ottenberg, Donald J., 3519 N. Broad St. (40)
1913. Outerbridge, George W., 1927 Spruce St.
1949. Padis, Nicholas, 255 S. 17th St.
1954. Palmer, Louis H., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1909. Parish, Benjamin Dores, R.D. # 1, Ambler, Pa.
1945. Park, Felix Roman, Medical Arts Bldg., Tulsa, Okla.
1940. Parker, Alan P., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1948. Parkhurst, Leonard Woods, 330 S. 9th St.
1944. Paschkis, Karl E., Jefferson Medical College.
1952. Paxson, Newlin F., 250 S. 18th St.
1932. Payne, Franklin L., Univ. of Pa. Hospital.
1954. Pearce, Alexander E., 1420 Race St. (2)
1958. Pearce, Rowan C., Jr., 514 Cooper St., Camden, N. J.

1943. Pearson, Gerald H. J., Presidential Apts.—Adams House.
1954. Pearson, Manuel M., 111 N. 49th St. (39)
1952. Peck, Roy I., 3400 Spruce St.
1930. Pendergrass, Eugene P., Univ. of Pa. Hospital.
1953. Penneys, Raymond, University of Pennsylvania Hospital. (4)
1914. Pepper, O. H. Perry, 945 Parks Run Lane, Villanova, Pa.
1916. Percival, Milton Fraser, 2332 S. Broad St.
1942. Perkins, William Harvey, 1025 Walnut St.
1946. Perloff, William Harry, 3521 N. Broad St.
1951. Perri, Angelo M., 814 Federal St.
1953. Persky, Abram H., 1737 Chestnut St. (3)
1940. Pessel, Johannes F., 224 West State St., Trenton, N. J.
1952. Peters, Michael, 262 W. Broad St., Telford, Pa.
1940. Pettit, Horace, Times Medical Bldg., Ardmore, Pa.
1949. Pettit, Mary DeWitt, 3343 W. Penn St. (29)
1915. Pfeiffer, Damon B., Meadowbrook, Pa.
1946. Pfeiffer, Mildred C. J., 358 Valley Rd., Merion, Pa.
1935. Phillips, Arthur W., 3904 Walnut St.
1911. Piersol, George Morris, 308 Kent Rd., Wynnewood, Pa.
1948. Pierson, Daniel B., Jr., 740 Beacon Lane, Merion, Pa.
1957. Pilling, George Platt, IV, 2600 N. Lawrence St. (33)
1933. Pillsbury, Donald M., Univ. of Pa. Hospital. (4)
1950. Pincus, Irwin J., 269 S. 19th St.
1957. Platt, Ruth M., 441 Lyceum Ave. (28)
1951. Poinsard, Paul J., 2031 Locust St.
1937. Polk, David Stewart, Rosemont, Pa.
1956. Pontarelli, Domenic J., 255 S. 17th St. (3)
1953. Porreca, George A., 1912 Spruce St. (3)
1932. Porter, Roland De Lance, Abington, Pa.
1953. Posey, William C., Jr., 18 West Ave., Wayne, Pa.
1951. Post, Joseph W., 1930 Chestnut St.
1951. Pote, Harry H., 4032 Walnut St.
1951. Pressman, Robert S., 170 W. Olney Ave. (20)
1947. Prickett, Joiin A., Warrington, Bucks County, Pa.
1954. Prince, Leon N., 2025 Spruce St. (3)
1931. Pryor, Charles Allen, 255 S. 17th St.
1952. Pugh, James E., 614 Church Lane, Yeadon, Pa.
1947. Putney, Floyd Johnson, 1719 Rittenhouse Sq.
1958. Rachlin, Lillian, 1737 Chestnut St. (3)
1943. Radbill, Samuel X, 7043 Elmwood Ave.
1953. Radbill, Sidney G., 37 S. 20th St. (3)
1945. Rakoff, Abraham Edward, 269 S. 19th St.
1953. Ralston, Edgar L., 3400 Spruce St. (4)
1931. Ramsey, Frank M., 620 E. Willow Grove Ave.
1953. Ranieri, Tito A., Bryn Mawr Medical Bldg., Bryn Mawr, Pa.
1941. Rankin, Charles A., Ludlow & Heather Rd., Upper Darby, Pa.
1946. Rapoport, Milton, Children's Hospital, 1740 Bainbridge St.
1951. Rathmell, Thomas K., 446 Bellevue Ave., Trenton, N. J.
1926. Ravdin, I. S., Univ. of Pa. Hospital. (4)
1956. Ravdin, Robert Glenn, 3400 Spruce St. (4)
1954. Reagan, Lindley B., 175 Madison Ave., Mt. Holly, N. J.
1928. Reese, Warren S., 2118 Locust St.
1920. Rehfuss, Martin E., 131 St. George's Rd., Ardmore, Pa.

1921. Reiff, E. Paul, 1927 Spruce St.
1919. Reimann, Stanley P., 703 W. Phil-Ellena St.
1956. Reishtein, William A., 255 S. 17th St. (3)
1951. Rentschler, Laurence B., 5800 Ridge Ave.
1945. Rhoads, Jonathan E., Univ. of Pa. Hospital. (4)
1951. Richardson, Fred Mac D., 160 Carpenter Lane.
1919. Richardson, Russell, Phila. Tuberculosis Sanatorium, # 4, Corinthian & Girard Aves.
1951 Riegel, Donald, 5110 Chester Ave.
1942. Riggs, Helena E., 150 Hewitt Rd., Wyncote, Pa.
1936. Ritter, Joseph A., 2405 N. 54th St.
1932. Robbins, Frederick R., 317 Milbank Rd., Bryn Mawr, Pa.
1952. Robbins, Robert, 3401 N. Broad St. (40)
1954. Roberts, Brooke, 3400 Spruce St. (4)
1939. Roberts, Ella, 133 S. 36th St.
1957. Roberts, Joan Mary, 3122 Midvale Ave. (29)
1899. Roberts, Walter, % W. B. Brosius, Berwyn, Pa.
1932. Robertson, Harold F., 2118 Pine St.
1954. Robertson, Hugh, 255 S. 17th St. (3)
1938. Roche, Philip Q., 255 S. 17th St.
1912. Rodman, John Stewart, 6 Matsonford Rd., Radnor, Pa.
1954. Roesler, Elizabeth Mertens-, 224 W. School House La. (44)
1955. Rogers, Fred B., 3401 N. Broad St. (40)
1934. Rogers, Harry L., 303 S. 10th St. (7)
1951. Ronis, Bernard J., 2106 Spruce St.
1948. Roscoe, Constantine R., 7226 Castor Ave.
1928. Rose, Edward, 426 Owen Rd., Wynnewood, Pa.
1936. Rose, Elizabeth Kirk, 426 Owen Rd., Wynnewood, Pa.
1952. Rose, S. Brandt, Chestnut Hill Hospital.
1946. Rosemond, George Parrott, 3401 N. Broad St. (40)
1948. Rothman, Maurice M., 1727 Spruce St.
1951. Rouse, George P., Jr., 2031 Locust St.
1952. Roxby, Bruce S., 5501 Greene St.
1955. Roxby, John B., Jr., 4821 Germantown Ave. (44)
1949. Royster, Henry P., 3400 Spruce St.
1941. Royster, Hubert A., Jr., The Mermont, Bryn Mawr, Pa.
1952. Rubin, I. Edward, 255 S. 17th St. (3)
1933. Rudolphy, Jay Besson, 230 S. 21st St.
1946. Rupp, Charles, 133 S. 36th St.
1947. Rush, Alexander, 330 S. 9th St.
1945. Rynes, Samuel E., 334 S. 21st St.
1952. Sain, Fletcher D., 8 Orchard Ave., Bristol, Pa.
1952. Salner, Nathan P., 6812 Castor Ave. (24)
1952. Saltzman, Maurice, 1923 Spruce St.
1944. Sampson, David Alan, 726 Braeburn Lane, Penn Valley, Narberth, Pa.
1954. Sampson, Martin C., 418 S. 47th St. (43)
1936. Sands, Joseph Evans, Rosemont, Pa.
1950. Sarner, Joseph B., 269 S. 19th St. (3)
1949. Saul, Leon J., Highland Ave., Media, Pa.
1908. Sautter, Albert C., Germantown Professional Bldg.
1954. Savacool, J. Woodrow, 146 W. Tulpehocken St. (44)
1947. Saÿen, John J., 506 Montgomery Ave., Haverford, Pa.
1948. Scarano, Joseph Albert, 1432 S. Broad St.
1917. Schaeffer, J. Parsons, Daniel Baugh Institute, 307 S. 11th St.

1929. Scheffey, Lewis C., 255 S. 17th St.
1942. Scheie, Harold G., 313 S. 17th St.
1929. Schenck, Harry P., 1235 Wyngate Rd., Wynnewood, Pa.
1945. Schlezinger, Nathan S., 255 S. 17th St.
1917. Schnabel, Truman G., 1704 Pine St.
1957. Schnall, Nathan, 2031 Pine St. (3)
1955. Schreader, Charles J., 318 Godfrey Ave. (20)
1952. Schulz, Norbert J., 1901 Walnut St.
1950. Schumann, Francis N., 8811 Germantown Ave.
1948. Schwarz, Gabriel A., 133 S. 36th St. (4)
1955. Schwegman, Cletus W., Hospital of the University of Penna. (4)
1930. Scott, John Porter, Children's Hospital, 1740 Bainbridge St.
1950. Scott, Michael, 255 S. 17th St.
1940. Scott, T. F. McNair, Children's Hospital, 1740 Bainbridge St.
1952. Seifer, Arthur F., 3401 N. Broad St.
1954. Seifter, Joseph, Wyeth Institute for Medical Research (1)
1957. Seipel, Russell C., 6000 Jefferson St. (31)
1951. Seitchik, Joseph N., 1417 Race St., Hahnemann Medical College Annex.
1952. Semisch, Charles W., III, 5329 Rising Sun Ave.
1958. Shafer, Albert H., 1004 E. Cherry Hill Apts., Merchantville 10, N. J.
1951. Shaffer, Bertram, 1825 Pine St.
1950. Sharp, Reuben L., 719 Cooper St., Camden, N. J.
1928. Sharpless, Frederick C., Beach Haven, N. J.
1956. Shaw, Daniel L., Jr., 702 Knox Rd., Villanova, Pa.
1948. Shay, Harry, 3400 N. Broad St.
1955. Shechter, Fred R., 1923 Spruce St. (3)
1954. Shelley, Walter B., 36th & Spruce Sts. (4)
1955. Shenkin, Henry A., 255 S. 17th St. (3)
1946. Shepherd, Samuel Garfield, 2039 Pine St.
1932. Sheridan, Joyce T., 412 W. Durham St.
1956. Sherson, Jacob S., 131 Channing Ave., Malvern, Pa.
1936. Shipman, James Shelby, 255 S. 17th St.
1935. Shoemaker, Robert, 3rd, 68 Byberry Rd., Hatboro, Pa.
1957. Shope, Edward Pierce Lentz, 807 Wilson Bldg., Camden, N. J.
1946. Shoup, George Daniel, 121 W. Walnut Lane. (44)
1955. Shubin, Harry, 6601 N. 21st St. (38)
1952. Shuman, Charles R., 3401 N. Broad St.
1936. Shuster, Benjamin H., 1824 Pine St.
1949. Sidlick, David M., 255 S. 17th St.
1941. Silcox, Louis E., Lankenau Medical Bldg. (31)
1956. Sillars, Charles H., Abington Memorial Hospital, Abington, Pa.
1955. Silverstein, Alexander, 2114 Pine St. (3)
1954. Singmaster, Lawrence, Lankenau Medical Bldg. (31)
1955. Sklaroff, David M., Einstein Medical Center. (41)
1952. Skromak, Stanley J., 5108 Torresdale Ave.
1929. Smith, Austin T., 1830 Spruce St.
1955. Smith, J. Winslow, 3034 Darby Rd., Ardmore, Pa.
1933. Smith, Lauren Howe, 111 N. 49th St.
1952. Smith, Richard T., 330 S. 9th St.
1927. Smyth, Calvin Mason, Abington Memorial Hospital, Abington, Pa.
1951. Snape, William J., 573 Stevens St., Camden, N. J.
1938. Snodgrass, L. E., 709 Walnut St. (6)
1953. Snyder, G. Gordon, Bryn Mawr Medical Bldg., Bryn Mawr, Pa.

1935. Sokoloff, Martin J., 255 S. 17th St.
1940. Soloff, Louis A., 255 S. 17th St.
1950. Somerville, William J., 2022 Locust St.
1935. Sommer, George N. J., 120 W. State St., Trenton N. J.
1944. Sommer, George N. J., Jr., 120 W. State St., Trenton, N. J.
1952. Sones, Maurice, Mt. Airy Medical Bldg.
1951. Sonneborn, Duane G., 1200 W. Erie Ave.
1928. Spaeth, Edmund B., 1930 Chestnut St.
1937. Spangler, John Luther, Devon, Pa.
1957. Spelman, Joseph Worcester, Dept. of Public Health Dev. Examiner, 13th & Wood Sts. (7)
1935. Spiegel, Ernest, 6807 Lawnton Ave., Oak Lane.
1955. Spitz, Eugene B., Children's Hospital (46)
1944. Stadie, William C., University of Pennsylvania Hospital. (4)
1957. Stanley, Robert C. G., 2315 Edgemont Rd., Chester, Pa.
1927. Starr, Isaac, 505 Cresheim Valley Rd.
1952. Stauffer, Herbert M., 3401 N. Broad St. (40)
1952. Stayman, Joseph W., Jr., Germantown Hospital.
1945. Stecher, H. Armin, 1510 Darby Rd., Havertown, Pa.
1955. Steel, Howard H., 3401 N. Broad St. (40)
1953. Steele, Brandt F., 1640 Pine St. (3)
1952. Steele, Eleanor A., 1640 Pine St.
1952. Steiger, William A., 3401 N. Broad St. (40)
1946. Stein, Irvin, 1936 Spruce St.
1953. Stein, Raymond O., 269 S. 19th St. (3)
1936. Steinfield, Edward, N. E. Cor. 18th and Chestnut Sts.
1942. Stengel, Alfred, Jr., 160 Hodge Rd., Princeton, N. J.
1951. Sterling, Julian A., 1008 Sharpless Rd., (26)
1948. Stevens, Lloyd W., 133 S. 36th St.
1925. Stokes, John H., 4228 Spruce St.
1928. Stokes, Joseph, Jr., Children's Hospital, 1740 Bainbridge St.
1943. Stokes, S. Emlen, 129 Chester Ave., Moorestown, N. J.
1954. Stone, Hrant H., E. Shawmont Ave. (28)
1952. Stoner, Emery K., 222 E. Mt. Pleasant Ave.
1953. Strawbridge, Rendall R., Lankenau Medical Bldg. (30)
1923. Strecker, Edward A., 111 N. 49th St.
1923. Stroud, William Daniel, 1011 Clinton St.
1937. Strumia, Max M., Penn Valley, Narberth, Pa.
1937. Sturgis, Margaret C., 349 Wistar Rd., Wynnewood, Pa.
1927. Sturgis, Samuel Booth, 349 Wistar Rd., Wynnewood, Pa.
1934. Summey, Thomas J., Burlington County Hosp., Mt. Holly, N. J.
1930. Sunderman, F. William, 1833 Delancey Place (3)
1936. Surver, James Miller, 1015 Walnut St.
1954. Sussman, Marcel S., 101 S. 20th St. (3)
1952. Sweeney, Francis X., 2351 E. Allegheny Ave. (34)
1944. Swenson, Paul C., 332 Cherry Lane, Wynnewood, Pa.
1955. Taggart, Harold A., 235 N. 15th St. (2)
1948. Tait, Edwin Forbes, 1324 Main St., Norristown, Pa.
1952. Talbot, Timothy R., Jr., 204 Booth Lane, Haverford, Pa.
1943. Tassman, Isaac S., 136 S. 16th St.
1946. Tauber, Robert, 2019 Walnut St.
1952. Taylor, Ann Gray, 6364 Germantown Ave.
1931. Taylor, Norman H., 100 W. Evergreen Ave.
1956. Templeton, John Y., III, 1025 Walnut St. (7)

1951. Theodos, Peter A., 1930 Chestnut St.
1946. Thomas, Carmen C., 1930 Chestnut St.
1952. Thompson, Charles M., 255 S. 17th St.
1927. Thorington, J. Monroe, 2031 Chestnut St.
1936. Thorp, Francis Quicksall, 4900 Penn St.
1936. Thudium, William J., 136 S. 16th St.
1954. Tindall, Dorothy D., 37 S. 20th St. (3)
1935. Tocantins, Leandro Maués, 1025 Walnut St.
1945. Toland, Joseph J., Jr., 1241 W. Lehigh Ave.
1935. Toland, Owen J., Episcopal Hospital, Front and Lehigh Ave.
1952. Tondreau, Roderick L., 6470 Drexel Rd. (31)
1953. Topping, Norman H., 3446 Walnut St. (4)
1949. Tornay, Anthony S., 37 S. 20th St.
1945. Tourish, William J., 250 S. 17th St.
1936. Towson, Charles Emory, Germantown Professional Bldg.
1955. Trimpi, Howard D., 1447 Hamilton St., Allentown, Pa.
1954. Trommer, Philip R., 258 S. 18th St. (3)
1956. Troncelliti, Mario V., Pennsylvania Hospital, (7)
1953. Tropea, Frank, Jr., 269 S. 19th St. (3)
1947. Trueman, Robert H., 1930 Chestnut St.
1954. Truitt, R. Marshall, Jr., 740 West View St. (19)
1926. Tucker, Gabriel, 429 Montgomery Ave., Haverford, Pa.
1938. Tuft, Louis, 1530 Locust St.
1933. Tumen, Henry J., 1900 Rittenhouse Sq.
1938. Turman, Christopher M., Wyncote, Pa.
1923. Turner, Creighton, H., 1731 Pine St.
1954. Turner, Linton W., 3401 N. Broad St. (40)
1952. Twining, H. Earl, 154 S. Broad St., Lansdale, Pa.
1929. Tyson, Ralph M., 255 S. 17th St.
1937. Uhle, Charles A. W., Lankenau Medical Bldg. (31)
1953. Ulin, Alexander W., 230 N. Broad St. (2)
1907. Ullom, Josephus T., Carpenter and Quincy Sts.
1950. Valdes-Dapena, Antonio, 40 Lokesley Rd., Merion, Pa.
1937. Vander Veer, Joseph B., 330 S. 9th St.
1937. Van Loon, Emily Lois, 1930 Chestnut St.
1933. Vastine, Jacob H., 2nd, 136 S. 16th St.
1958. Velkoff, Cyril L., 2100 Walnut St. (3)
1955. Viek, Peter, 1400 York Road, Abington, Pa.
1952. Vischer, Thomas J., 5903 Greene St.
1940. Voegelin, Adrian W., Germantown Professional Bldg.
1941. Vogel, Stoughton R., 151 W. Tulpehocken St.
1927. Wagers, Arthur J., 1429 Spruce St.
1949. Wagner, Frederick B., Jr., 800 Chauncy Road, Narberth, Pa.
1949. Wagner, Joseph A., 201 Highland Ave., Bryn Mawr, Pa.
1954. Wainer, Amos S., 1621 Spruce St. (2)
1938. Waldman, Joseph, 404 Meadowbrook Lane.
1955. Waldron, Jerome M., 330 S. 9th St. (7)
1932. Walkling, Adolph A., 136 S. 16th St.
1955. Warner, Halsey F., 100 W. Coulter St. (44)
1956. Watkins, E. Lloyd, 8815 Germantown Ave. (18)
1954. Waugh, Elizabeth S., 348 Green Lane. (28)
1952. Weaver, Harry S., Jr., 37 S. 20th St.
1955. Weaver, Robert L., 530 Walnut St. (5)

1941. Weaver, Ruth H., 2601 Parkway.
1953. Weber, Lennard L., 255 S. 17th St. (3)
1957. Webster, Marie Blanchefield, 5428 N. 5th St.
1930. Weeder, S. Dana, 250 W. Tulpehocken St.
1920. Weidman, Fred D., 20 Tenby Rd., Havertown, Pa.
1954. Weiner, Louis H., 4025 Girard Ave. (4)
1952. Weinstein, George L., 255 S. 17th St.
1954. Weinstock, Horace L., 329 S. 18th St. (3)
1923. Weiss, Edward, 269 S. 19th St.
1950. Weiss, Sidney, 1930 Chestnut St.
1951. Welty, Jack W., Montgomery Ave. & Owen Rd., Wynnewood, Pa.
1955. Wendkos, Martin H., 4015 Baltimore Ave. (4)
1935. Whelan, G. L., 2100 Walnut St.
1921. Whitaker, William, 4645 Oakland St.
1936. White, Ellen Pawling Corson-, Gladwyne, Pa.
1925. Widmann, Bernard P., 250 S. 18th St.
1954. Wieder, Henry S., Jr., 330 S. 9th St. (7)
1939. Willauer, George, 6129 Greene St.
1907. Williams, Carl, School Lane and Greene St.
1937. Williams, John C., 6370 Germantown Ave.
1920. Williams, Philip F., 353 Bala Ave., Bala-Cynwyd, Pa.
1950. Williams, R. G., Univ. of Pa. School of Medicine.(4)
1927. Williamson, Ernest G., 6353 Woodbine Ave.
1949. Willson, J. Robert, 3401 N. Broad St. (40)
1921. Wilson, George, 133 S. 36th St.
1945. Wilson, John F., 2013 Delancey Pl.
1953. Wilson, Julius L., Henry Phipps Institute, 7th & Lombard Sts. (47)
1937. Wilson, Ross B., Lankenau Medical Bldg. (31)
1949. Wilson, William W., 133 S. 36th St.
1957. Winkelman, N. William, Jr., 1930 Chestnut St. (3)
1948. Winston, Julius, 5839 Chester Ave.
1941. Wirts, C. Wilmer, 2017 Delancey St.
1957. Witkow, Alexander, Div. of Prev. Med., Dept. of Public Health, Room 519, City Hall Annex (7)
1953. Wohl, George T., 1227 Remington Rd., Wynnewood, Pa.
1933. Wohl, Michael G., 1727 Pine St.
1944. Wolf, Lewis R., 3474 Frankford Ave.
1918. Wolferth, Charles C., 133 S. 36th St.
1957. Wolgamot, John R., 244 W. Main St., Moorestown, N. J.
1957. Wolkowicz, Michael I., 2022 Spruce St. (3)
1942. Wolman, Irving J., 7607 Woodlawn Ave. (26)
1893. Wood, Alfred C., 2035 Walnut St.
1950. Wood, Dorothy D., 2035 Walnut St.
1932. Wood, Francis C., 212 Laurel Lane, Haverford, Pa.
1903. Wood, Horatio C., 319 S. 41st St.
1944. Wood, H. Curtis, Jr., Skippack Pk., Whitemarsh, Pa.
1953. Woodruff, Marston T., 4940 Penn St. (24)
1928. Wright, Carroll S., 1402 Spruce St.
1921. Ylvisaker, Lauritz S., Fidelity Mutual Life Ins. Co., Parkway at Fairmount, (30)
1941. Young, Barton R., Germantown Hospital.
1953. Zarafonetis, Chris J. D., 3401 N. Broad St. (40)
1957. Zaslow, Jerry, 1351 Tabor Rd. (41)
1955. Zatuchni, Jacob, 3401 N. Broad St. (40)
1946. Zeigerman, Joseph H., 1836 Delancey St.

1894. Zentmayer, William, 265 Forrest Rd., Merion, Pa.
1949. Zintl, William J., Upper Darby, Pa.
1956. Ziserman, Abraham J., 2046 Pine St. (3)
1933. Zulick, J. Donald, Abington Memorial Hospital, Abington, Pa.

Non-Resident Fellows

ELECTED

1912. Addison, William H. F., 286 East Sidney Avenue, Mt. Vernon, N. Y.
1947. Allbritten, Frank F., Jr., Univ. of Kansas Medical Center, Kansas City 3, Kansas.
1941. Aronson, Roland S., Walter Reed Army Hospital, Washington 12, D. C.
1954. Austin, George M., University of Oregon Medical School, Portland, Oregon
1934. Bank, Joseph, 800 N. First Ave., Phoenix, Arizona.
1931. Bates, William, Harrisburg Hospital, Harrisburg, Pa.
1932. Behney, Charles A., Dept. of Health, Old DeWitt Rd., Lansing, Mich.
1949. Bixby, Edward W., Casey Key, R.D. Box 31-13, Nokomis, Fla.
1951. Blank, Harvey, Jackson Memorial Hospital, Miami 36, Fla.
1937. Braceland, Francis J., The Institute of Living, 200 Retreat Ave., Hartford, Conn.
1951. Brinton, S. Jervis, 115 92nd St., Stone Harbor, N. J.
1936. Brown, Charles L., 591 Montgomery St., Jersey City. (2)
1948. *Brown, Robert B., U. S. Naval Hospital, Bethesda, Md.
1953. Burbidge, J. Raymond, 163 Nassau St., Princeton, N. J.
1957. Butterworth, Thomas, 411 Walnut St., Reading, Pa.
1908. Cadbury, William W., 274 W. Main St., Moorestown, N. J.
1948. Chapman, John P., Hotel Virginia, Palma de Mallorca, Balearic Islands, Spain.
1950. Chapple, Charles C., 1530 - 16th St., Washington, D. C.
1941. Cheleden, John, 133 Broadway, Daytona Beach, Fla.
1930. Clarke, Francis Mann, 116 New St., New Brunswick, N. J.
1926. Clerf, Louis H., 5575–8th Ave., North, St. Petersburg, Fla.
1930. Cottrell, James E., McGuire Veteran's Administration Hospital, Richmond 19, Va.
1940. Crowe, Aldrich C., 1208 Ocean Ave., Ocean City, N. J.
1947. Cutler, Norman L., 1300 Harrison St., Wilmington, Del.
1941. *Cuttle, Tracy D., U. S. Naval Hospital, Oakland 14, Calif.
1955. Daugherty, J. Arthur, 610 N. Third St., Harrisburg, Pa.
1954. Deitrick, John E., Cornell Medical College, 1300 York Ave., New York 21, N. Y.
1941. Dixon, Harold M., 8511 Antler Drive, St. Louis, Mo.
1953. Eberhard, Theodore P., St. Joseph Mercy Hospital, Ann Arbor, Mich.
1955. Edwards, Margaret Hay, 324 W. State St., Trenton, N. J.
1951. Ellis, Mackinnon, Mountain Home Veteran's Hospital, Mountain Home, Tenn.
1957. *Errion, Arthur Robbins, U. S. Naval Hospital, Key West, Fla.
1951. Ervin, Carl E., 240 North Third Street, Harrisburg, Pa.
1944. Estes, W. L., Jr., Bethlehem, Pa.
1952. Faller, Constantine P., 127 State St., Harrisburg, Pa.
1940. Forrester, James S., Harrisburg Polyclinic Hospital, Harrisburg, Pa.
1946. Forster, Francis M., Georgetown University Hospital, Washington, D. C.
1951. Friedland, Carl K., 271 W. Blackwell St., Dover, N. J.
1947. Gaskill, Herbert S., 250 Ash St., Denver, Colorado.
1913. Gates, Nathaniel, 10 Peterboro, Detroit, Mich.
1957. Giering, John Fleming, 84 James St., Kingston, Pa.

* Military service.

1931. Gilman, Robert Louis, Cheyney, Pa.
1954. Godfrey, Ellwood W., Princeton Hospital, Princeton, N. J.
1928. Gordon, Burgess L., The Lovelace Foundation, Albuquerque, New Mexico.
1947. Grady, Hugh G., Armed Forces Institute, Washington, D. C.
1952. Grieco, Reynold M., 2 W. 4th St., Williamsport, Pa.
1952. Gross, Elmer R., 817 W. Street, Wilmington, Del.
1933. Gruber, Charles M., School of Medicine, College of Medical Evangelists, Loma Linda, Calif.
1936. Guthrie, Donald, 118 S. Wilbur Ave., Sayre, Pa.
1955. Harris, John H., 1301-A N. Second St., Harrisburg, Pa.
1936. Hatch, Lerleen Clement, 2184 Ayres Ave., Akron, Ohio.
1928. Hayman, Joseph Marchant, Jr., Tufts College Medical School, Boston, Mass.
1944. Hershey, J. Ivan, VA Hospital, Shreveport, La.
1955. Hills, Arthur G., 1000 N. W. 17th St., Miami, Fla. (36)
1933. Hitzrot, Lewis H., Medical Director, Mercersburg Academy, Mercersburg, Pa.
1950. Horn, Robert C., Henry Ford Hospital, Detroit, Mich.
1938. Howell, John C., 1104 Logan Ave., Tyrone, Pa.
1936. Hughes, Brady A., 312 Euclid Ave., Mt. Brook, Birmingham, Ala.
1953. Imber, Irving, 420 Walnut St., Reading, Pa.
1921. Ivy, Robert H., 104 Dalton Rd., Paoli, Pa.
1952. Jones, Ralph Jr., Jackson Memorial Hospital, Miami, Fla.
1955. Jordan, Charlotte B., 519 Sarah St., Stroudsburg, Pa.
1955. Jordan, Claus G., 519 Sarah St., Stroudsburg, Pa.
1956. Keffer, William H., 413 Oley St., Reading, Pa.
1947. Kelchner, Clyde H., 1125 Turner St., Allentown, Pa.
1944. LaMotte, William O., Brook Hill Farms, Hockessin, Del.
1954. LaMotte, William O., Jr., Professional Bldg. Wilmington 3, Del.
1952. Levan, John B., 401 Oley St., Reading, Pa.
1949. Lhamon, William T., Baylor University College of Medicine, Houston, Tex.
1954. Light, John J. B., 25 N. 9th St., Lebanon, Pa.
1954. Lindenmuth, Woodrow W., VA Hospital, West Haven, Conn.
1948. Livingood, Clarence S., Henry Ford Hospital, Detroit 2, Mich.
1933. Long, Esmond R., Conifer, Pedlar Mills, Va.
1948. McCall, Milton L., Louisiana State Univ., New Orleans, La.
1937. McGuinness, Aims C., Room 5238, Dept. of Health, Education & Welfare, Washington, D. C.
1948. McLaughlin, John T., 1252 S. Central Ave., Glendale, Calif.
1949. Manlove, Francis R., 6015 E. 17th Ave., Denver, Colo.
1953. Margolies, Michael, 567 E. Chestnut St., Coatesville, Pa.
1955. Margolies, M. Price, 567 E. Chestnut St., Coatesville, Pa.
1935. Mason, James B., 40 E. Erie St., Chicago 11, Ill.
1932. Meade, Richard H., Jr., 750 San Jose Dr., Grand Rapids, Mich
1936. Middleton, William Shainline, Veterans' Administration, Washington, D. C.
1946. Miller, Franklin R., Snyder-Jones Clinic, Winfield, Kansas.
1928. Moon, Virgil H., Univ. of Miami, Coral Gables, Fla.
1949. Motley, Hurley L., 1212 Shatto St., Los Angeles, Calif.
1950. Neefe, John R., 627 Eleventh St., St. Petersburg, Fla.
1937. Nicholson, Samuel T., 2d., 642 High St., Pottstown, Pa.
1941. Nisbet, Verner, 714 Queens Rd., Charlotte 7, N. C.
1956. Oppenheimer, Albert, 224 E. Main St., Moorestown, N. J.
1926. Paul, John Rodman, Dept. Preventive Medicine, Yale University, New Haven, Conn.
1947. Pearce, Louise, Trevenna Farms, Orchard Rd., Skillman, N. J.

---

* Military service.

1922. Pleasants, Henry, West Chester, Pa.
1953. Raffensperger, Edward C., 2039 N. 2nd St., Harrisburg, Pa.
1938. Read, Hilton S., 5407 Atlantic Ave., Atlantic City, N. J.
1936. Reisinger, John A., 901 20th St., N. W., Washington, D. C.
1955. Rettew, Philip L., 612 Museum Rd., Reading, Pa.
1954. Roberts, Norbert J., Standard Oil Co., 30 Rockefeller Plaza, Room 2400, New York 20, N. Y.
1947. Rogers, Arthur Merriam, 1351 Durwood Drive, Charlotte, N. C.
1907. Royer, B. Franklin, 429 E. Baltimore St., Greencastle, Pa.
1956. Rubenstone, Albert I., Michael Reese Hosp., Chicago, Ill.
1953. Scanlan, Robert L., St. Vincent's Hospital, 2131 W. 3rd St., Los Angeles 57, Calif.
1945. Schell, James F., 139 W. Maple Ave., Langhorne, Pa.
1928. Schofield, Frederick S., Veteran's Admin. Hospital, Fort Wayne, Ind.
1921. Schumann, Edward A., "Henneberg", Chalfont, Pa.
1913. de Schweinitz, George L., 3231 Arroyo Chico, Tucson, Ariz.
1941. Shands, Alfred R., Jr., Alfred I. duPont Institute, Rockland Rd., Wilmington, Del.
1908. Shannon, Charles E. G., 9 Park St., Waterville, Maine.
1950. Shiffer, Paul H., Dreher Ave., R.D. #2, Stroudsburg, Pa.
1951. Shorey, Winston K., Jackson Memorial Hospital, Miami, Fla.
1932. Siegel, Alvin Erdreich, Medical Arts Building, Macon, Ga.
1933. Smelzer, Donald C., Lancaster General Hospital, Lancaster, Pa.
1954. Smith, Charles W., 121 State St., Harrisburg, Pa.
1929. Sponsler, Marshall B., 103 Lansdowne Road, DeWitt, N. Y.
1955. Stevenson, Theodore D., Presbyterian Board of Foreign Missions, 156 Fifth Ave., New York 10, N. Y.
1934. Stewart, Sloan G., Pacific and North Carolina Avenues, Atlantic City, N. J.
1931. Stiles, Merritt H., 104 5th Ave., Spokane 4, Wash.
1949. Stockwell, Eunice L., Tryon, N. C.
1953. Stroud, Morris W., 3rd Harvard Rd., Cleveland, Ohio
1928. Thomas, J. Earle, College of Medical Evangelists, School of Medicine, Loma Linda, Calif.
1942. Thompson, Wesley D., 18 N. Main St., Lewistown, Pa.
1941. Tompkins, Pendleton, 450 Sutter St., San Francisco, Calif.
1947. Vastine, Mary F., R.D. #2, Biglerville, Pa.
1912. Vaux, Norris W., Chateau Crillon, Phila. 3.
1897. Veasey, Clarence A., 1118 W. 9th Ave., Spokane 9, Wash.
1931. Walker, Herschel Carey, 320 Park Ave., New York City, N. Y.
1936. Wilder, Theodore S., Beckley Memorial Hospital, Beckley, W. Va.
1933. Waygood, James L., Pocono Pines, Pa.
1935. Willard, John H., Harlan Memorial Hospital, Harlan, Kentucky.
1952. Wood, Horatio C., III, 5319 Prospect Rd., Peoria, Ill.
1947. Zintel, Harold A., St. Luke's Hospital, Amsterdam Ave. & 113th St., New York 25, N. Y.

Honorary Fellows

Limited to Fifty, of Whom Twenty May Be Foreigners

American

elected

1917. Miner, Charles Howard, b.s., m.d., Member of Board of Directors, Wilkes-Barre General Hospital; Board of Health, Wilkes-Barre; Board of Directors, White Haven Sanatorium Association and Penna. Tuberculosis Society. 264 S. Franklin St., Wilkes-Barre, Pa.
1936. Richards, Alfred Newton, ph.d., sc.d., m.d. (hon.), ll.d., Emeritus Professor of Pharmacology, School of Medicine, and Associate Trustee, University of Pennyslvania.

1942. Russell, Frederick Fuller, M.D. Brig. Gen. Med. Corps, U.S.A. (Ret.). Lime Kiln Lane, Route 1, Box 488R, Louisville, Kentucky.
1947. Stone, Robert Spencer, M.D., University of California Medical School, San Francisco, Cal.

Foreign

1937. Dale, Sir Henry Hallett, C.B.E., F.R.S., M.A., M.D., F.R.C.P., 52 Queen Anne St., London, W. 1, England.
1922. McCarrison, Sir Robert, Kt., C.B.E., M.D., D.SC., LL.D., F.R.C.P., Major-General, Indian Medical Service (retired). 18 Linton Rd., Oxford, England.
1955. Mann, Ida, M.A., D.SC., M.B., B.S., L.R.C.P., D.O.M.S., F.R.C.S., Ophthalmic Consultant to the Government of W. Australia, 56 Hobbs St., Nedlands, Perth, W. Australia.

Honorary Associate Fellows

1955. Clement, Martin W., 1964 Surburban Station Bldg. (3)
1955. Diemand, John A., President, Insurance Company of North America, 1600 Arch St. (2)

Necrological List

Resident Fellows	*Date of Election*	*Date of Death*
Barnard, Everett P.	November 1, 1911	November 2, 1957
Bromer, Ralph S.	November 7, 1917	September 25, 1957
Cadwalader, Williams B.	November 6, 1907	May 31, 1957
Curtis, Lawrence	October 6, 1937	June 8, 1957
Leopold, Simon S.	January 7, 1920	July 13, 1957
Lownes, John B.	May 6, 1942	February 22, 1957
Mecray, Paul M.	January 8, 1934	February 13, 1957
Rothrock, Harry A.	May 5, 1932	April 4, 1957
Roxby, John Byers	January 11, 1937	March 19, 1957
Schoff, Charles H.	January 3, 1917	October 25, 1957
Stewart, Winifred B.	March 5, 1941	August 20, 1957
Wagoner, George W.	May 7, 1928	April 29, 1957
Weiss, Benjamin P.	May 8, 1933	February 18, 1957
Yawger, Nathaniel S.	October 13, 1943	June 2, 1957
Zillessen, Frederick O.	April 1, 1952	June 1, 1957
Non-Resident Fellows		
Camero, A. Roland	January 6, 1936	July 20, 1957
Vail, William Penn	January 1, 1913	June 22, 1957
Willard, De Forest P.	May 6, 1914	October 3, 1957

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a. which sum shall be used for the general purposes of said association;

b. which sum shall be added to and become a part of the general endowment fund of said association;

c. which sum shall be used by said association preferably for the following purposes:

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1957

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